Experimental Eye Research 129 (2014) 135–150

Contents lists available at ScienceDirect

Experimental Eye Research

journal homepage: www.elsevier.com/locate/yexer

Review

Oxidative photodegradation of ocular tissues: Beneficial effects of filtering and exogenous antioxidants

Billy R. Hammond [a, *], Bart A. Johnson [b], Eric R. George [b]

[a] Vision Sciences Laboratory, University of Georgia, Athens, GA 30602-3013, USA
[b] Johnson & Johnson Vision Care, Inc., 7500 Centurion Parkway, R&D 3rd Floor W3A, Jacksonville, FL 33256, USA

ARTICLE INFO

Article history:
Received 27 June 2014
Accepted in revised form 13 September 2014
Available online 16 September 2014

Keywords:
Oxidative photodegradation
Proteins
Lipids
Ocular phototoxicity
Filters
Antioxidants

ABSTRACT

The fact that light is necessary for life is generally accepted as an axiom. The extent to which light interacts and influences human biology, however, is often not fully appreciated. Exposure to sunlight, for instance, can both promote and degrade human health. There is now general scientific consensus that, although the eye evolved to respond to light, it is also damaged by excessive exposure. Light-mediated ocular damage is involved in the pathophysiology of many common forms of blindness. The type of ocular tissue damage induced by light exposure depends on the extent of exposure and wavelength. The tissues of the lens, cornea, and retina contain specific chemical moieties that have been proven to exhibit light-mediated oxidative degradation. Proteins and lipids present in the cornea, lens, and retina, meet all of the physical requirements known to initiate the process of oxidative photodegradation upon exposure to solar radiation. As such, different mechanisms have evolved in the lens, cornea, and retina to ameliorate such light-mediated oxidative damage. It appears, however, that such mechanisms are ill-matched to handle modern conditions: namely, poor diet and longer life-spans (and the degenerative diseases that accompany them). Hence, steps must be taken to protect the eye from the damaging effects of light. Preventative measures include minimizing actinic light exposure, providing exogenous filtering (e.g., through the use of protective lenses), and enhancing antioxidant defenses (e.g., through increased dietary intake of antioxidants). These strategies may yield long-term benefits in terms of reducing oxidative photodegradation of the ocular tissues.

1. Introduction

The absorption of visible light in the retina and the subsequent chemical conversions are the first sept in all subsequent visual processing (Wald, 1945; Tang et al., 2013). This very exposure, however, may also be associated with pathological consequences. Actinic light exposure is central to the pathophysiology of the most common forms of blindness (Young, 1992). Age-related cataract, for instance, is the leading cause of blindness in the world and UV-mediated modification of crystalline lens proteins is a primary event in its development. Age-related macular degeneration (AMD) is the leading cause of blindness in the developed world. Epidemiological data in the USA indicate an overall prevalence (>40 years of age) of AMD of 6.5% (Klein et al., 2011). A recent meta-analysis of 14 studies by Sui et al. (2013) showed an average increase of AMD risk due to sunlight exposure of about 38% (OR = 1.379, 95% CI ranging from 1.091 to 1.745, $P = 0.007$).

The very existence of life on earth is dependent upon light from the sun. Not all energy arising from our sun, however, is incident on the planet surface. As shown in Fig. 1, electromagnetic energy from the sun extends from around 200 to over 2500 nm. Exposure to the very high-frequency end of that continuum (cosmic radiation) is a significant factor in the disease risk of astronauts (e.g., Cherry et al., 2012). Fortunately, the earth's magnetic field and atmosphere (ozone) absorb or reflect nearly all of the electromagnetic energy below about 260 nm (Norval et al., 2007). The very energetic waveband between about 260 and 400 nm does make it to the surface (about 97% of that is UVA, 315–400 nm). The amount present at any given time, however, varies dramatically depending on altitude, latitude, time of day, season and local weather conditions. Fig. 2 demonstrates these large changes as measured during different seasons and climate regions in China.

The impact of light on the eye and the ocular tissues affected are influenced by both the degree of UV exposure and the wavelength of the light entering the eye. An immediate challenge when

* Corresponding author.
E-mail addresses: bhammond@uga.edu (B.R. Hammond), EGeorge1@its.jnj.com (E.R. George).

http://dx.doi.org/10.1016/j.exer.2014.09.005

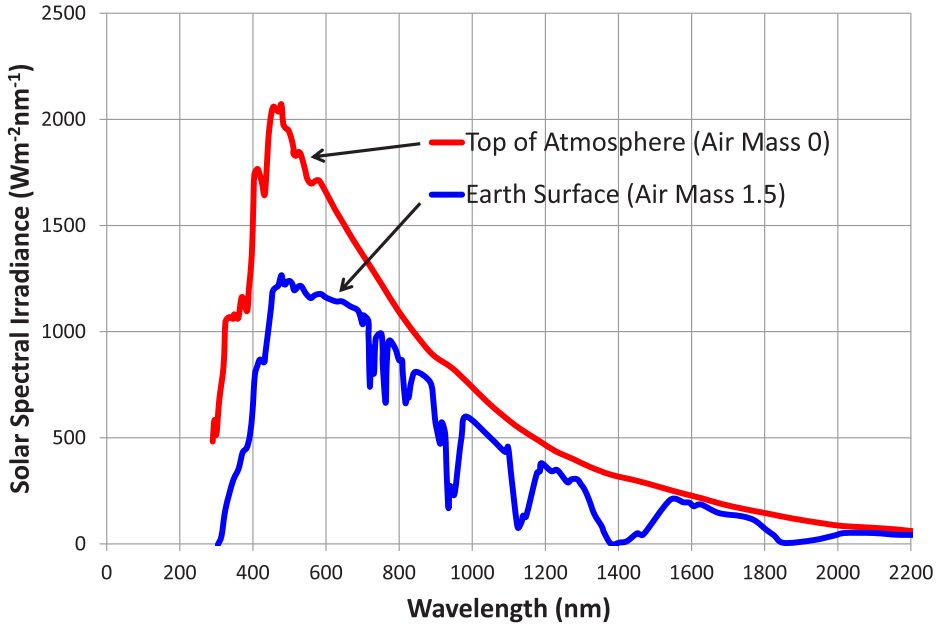

Fig. 1. Solar spectral irradiance (derived from Mecherikunnel and Richmond, 1980).

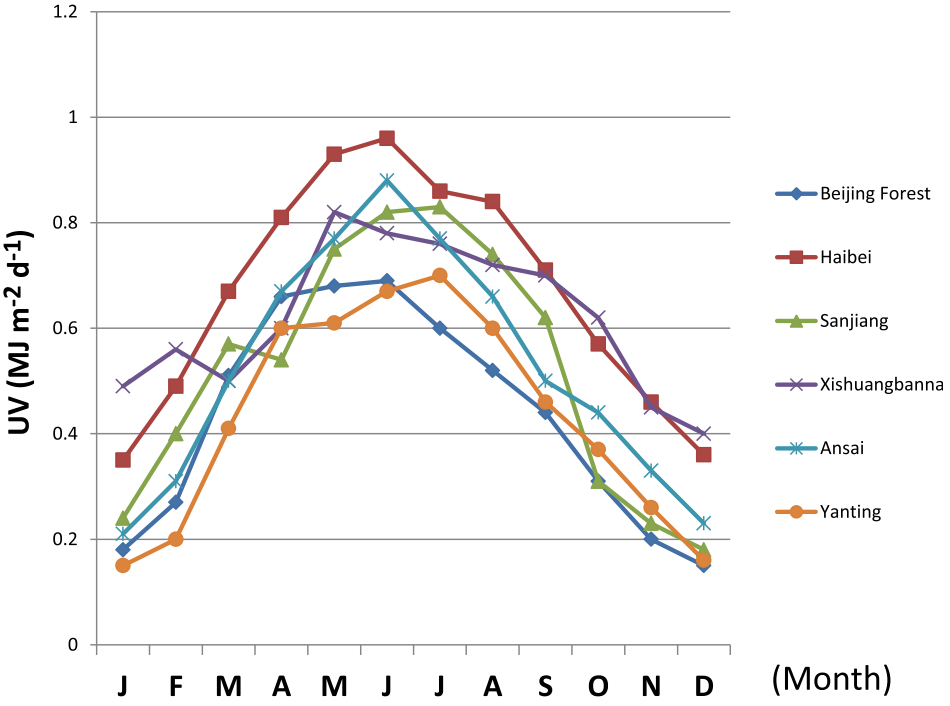

Fig. 2. Monthly average daily UV radiation measured at different locations throughout China (derived from Bo et al., 2010).

evaluating an actinic role of light is quantifying exposures that can vary so tremendously. For example, Sasaki et al. (2011) recently assessed the validity of one common measure of exposure: the solar UV index. They found that the index was, essentially, invalid as a measure of ocular risk because the model is based on such a limited number of dependent variables: exposure estimates, for instance, were limited to ambient solar radiation impinging on an unobstructed horizontal plane (e.g., the top of the head). The timing of the measurement is critical; daily UV exposures vary tremendously by time of year and even throughout the day. For instance, measurements taken in Kanazawa, Japan indicated that the peak ocular exposure occurring for most of the year was not at solar noon, as would be predicted by the UV index, but at mid-morning and mid-afternoon. This is due to the increase in direct and reflected sunlight into the eye at lower solar angles, and the occlusion of the sun at higher solar angles by the superior orbital rim of the eye socket and eyebrow (Merriam, 1996). Fig. 3 summarizes these results and illustrates the inherent photo-protection

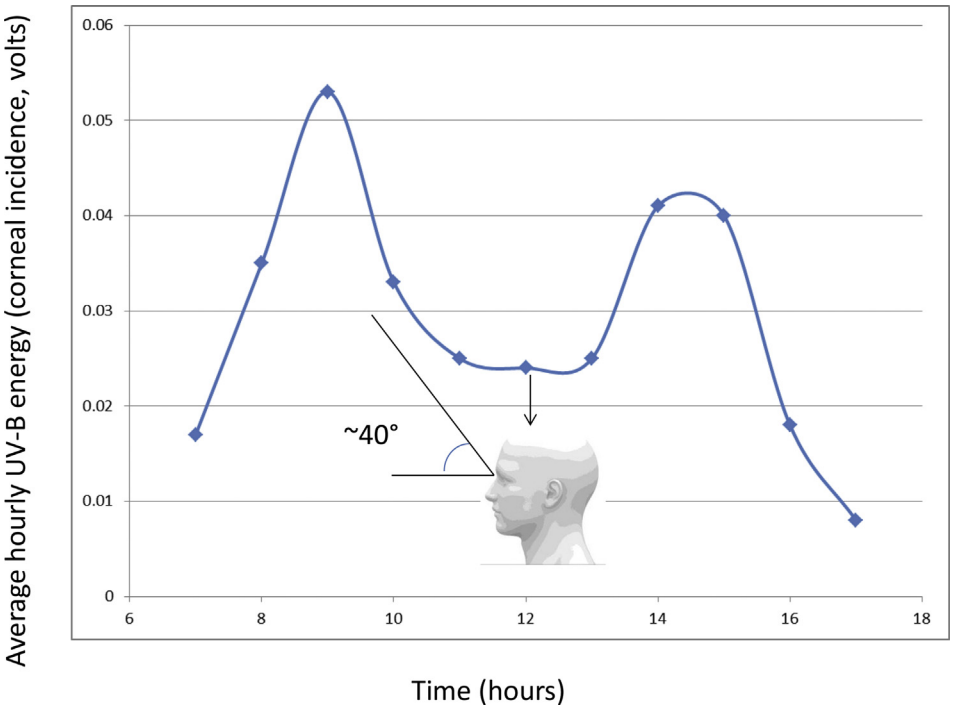

Fig. 3. The average irradiance of the eye as a function of time of day (derived from Sasaki et al., 2011). The energy measurements were made at the right eye of a mannequin facing the sun on a relatively clear fall day. Note that the peak energy of the sun is around Noon (e.g., the amount striking the top of the head) but the maximum entering the eye is around 9 AM. This is due (as illustrated) to the solar altitude being at the optimal angle (~40°) for entering the eye. The skull (e.g., supra-orbital ridges), eye brows, and eyelids protect the eye when the sun is closer to zenith.

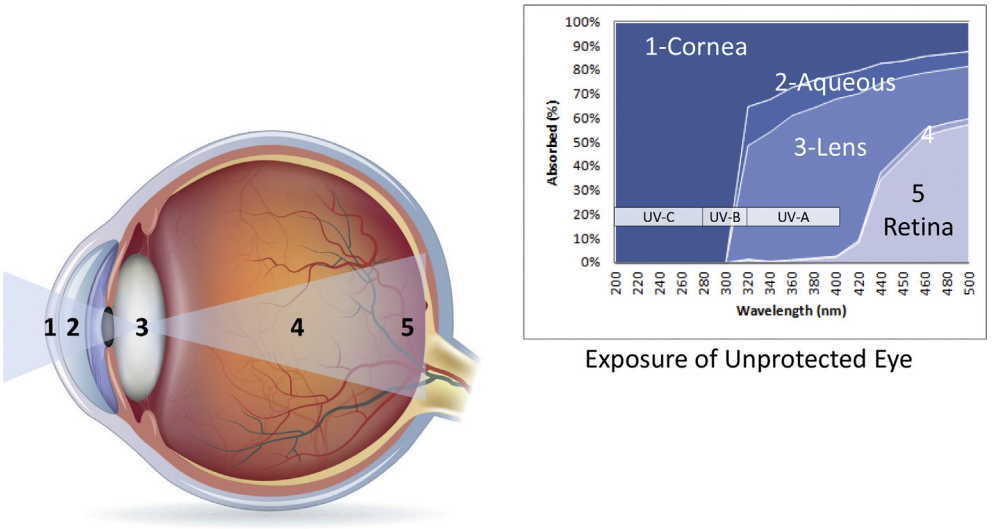

Fig. 4. The penetration of wavelength within the ocular orbit (derived from Boettner and Wolter, 1962).

of the eye provided by the evolved shape of the human head. The peak ocular exposure time shifts in the fall and winter to solar noon, as the maximum daily solar altitude drops below this occlusion angle (Sasaki et al., 2011). Sui et al. (2013) recently noted that many of the differences found across studies on the effects of sunlight on the incidence of AMD were attributable to a failure to control for differences due to factors such as gross domestic product and latitude.

When accounting for potentially noxious effects of light, one must therefore consider how light enters the eye. Light can enter the eye either directly or obliquely, with both likely having different clinical significance. For example, UV radiation entering obliquely from the temporal side (which is mostly blocked on the opposite side by the nose; Coroneo, 2011) can reach the cornea, which contains the more lipid-and-oxygen rich epithelial cells (around the medial limbus), and the lens (aided by focusing from the cornea). Such light is strongest at 40° solar altitude and has been strongly implicated (Chao et al., 2013) in the development of pinguecula and pterygium (benign growths of the conjunctiva). Since it is UV radiation coming in unobstructed from the side, sunglasses

with side-shields are often recommended to help prevent this disorder.

Once light impinges on the corneal surface, how that light will interact with ocular tissues is largely determined by wavelength because the depth of penetration is largely, and positively, related to wavelength. The anterior portions of the eye (the cornea and the crystalline lens) absorb UV most strongly: primarily UVB (280–315 nm) and UVA (315–400 nm) (Bachem, 1956). The cornea absorbs 60%–100% of the UVB but only about 20%–40% of the UVA. The lens absorbs most radiation up to 360 nm, allowing a significant proportion of UVA, visible (400–700 nm), and infrared radiation to reach the retina (Boettner and Wolter, 1962; Dillon et al., 2004; Gaillard et al., 2011; van Norren and Vos, 1974; Pitts and Tredici, 1971; Savage et al., 2001; van de Kraats and van Norren, 2007a,b). Although infrared may reach the retina, and may pose a risk during intense exposures, anterior tissues such as the lens appear most often affected (Voke, 1999), and then only when infrared levels are exceptionally high (as can happen with some occupations; hence descriptors such as glass-blower's cataract). More subtle long-term influences are possible since heat can both denature proteins and raise the overall energy state of tissue such that it is more susceptible to photo-oxidative damage. For example, it has been argued that heat transfer from the iris (via the vasculature) may be one reason why individuals with darker irises are more susceptible to cataracts (Pitts and Cullen, 1981).

Although the retina is exposed to all of the visible range, the most severe retinal damage is likely to result from the effects of the shorter wavelengths (400–500 nm); this is commonly known as the "blue-light-hazard." The penetration of the various wavebands of light into the ocular orbit is illustrated in Fig. 4.

To mitigate the risks of damage to ocular structures associated with light exposure, two main strategies (other than avoiding exposure) have emerged: simple filtering and increasing the antioxidant protection of tissues. The efficacy of filtering strategies could potentially be evaluated using the ocular ambient exposure ratio (OAER), which quantifies the ratio of ocular to ambient light exposure for a given individual. When the OAER was measured in outdoor workers using polysulfone UV (295–320 nm) sensitive film, it ranged from as low as 2% to as high as 17% (Rosenthal et al., 1988). This variation depended on hat wear, the job performed, and the time of the year. In another study, the OAER, which was determined at the surface of the eye by contact lenses produced from UV sensitive material, ranged from 4% to 23% during 4 wearing trials (Sydenham et al., 1997).

Such studies have shown that ocular exposure to actinic light results from a combination of both external (e.g., time of day) and personal (e.g., hat wear) factors (Sliney, 2011). These factors can be summarized as:

- Season
- Time of day
- Altitude
- Latitude and longitude
- Occupation
- Hat wear
- Solar altitude
- Other factors

The second strategy for ameliorating light damage, increasing the antioxidant protection of tissues, may involve both endogenous and exogenous antioxidants. We, like other animals, evolved in an environment with about 21% oxygen and sunlight. Oxygen in the atmosphere is typically inert, but may be converted into more reactive forms capable of damaging biological tissue by an energy source, such as light. Light is often focused directly on retinal tissue, which is particularly vulnerable to oxidative damage (Różanowska et al., 1998; Gaillard et al., 2011; Hunter et al., 2012; Margrain et al., 2004). The susceptibility of the retina to light-initiated oxidative damage increases with age, as the retina/retinal pigment epithelium (RPE) complex accumulates a higher amount of photosensitizers (like lipofuscin (Margrain et al., 2004; Carson et al., 2008)) (although, simultaneously, the yellowing of the lens and formation of cataract reduce light reaching the retina). The human eye has evolved to utilize an elegant array of antioxidants to protect it from light-initiated oxidative damage. These antioxidants are distributed to optimize both protection and function.

The effects of light on ocular tissues (photodegradation) can be explained mechanistically by studying the direct effects of energetic light on the kind of proteins and lipids that dominate the composition of the various tissues of the eye.

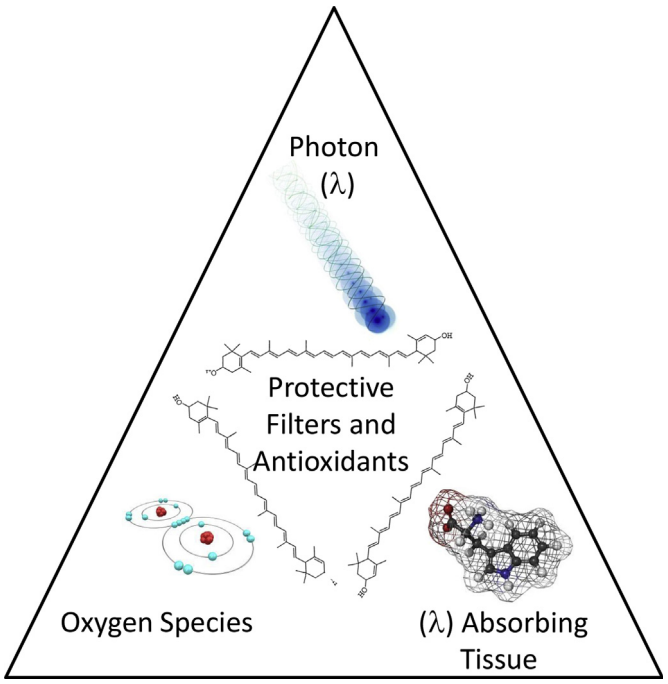

Fig. 5. Oxidative photodegradation triangle.

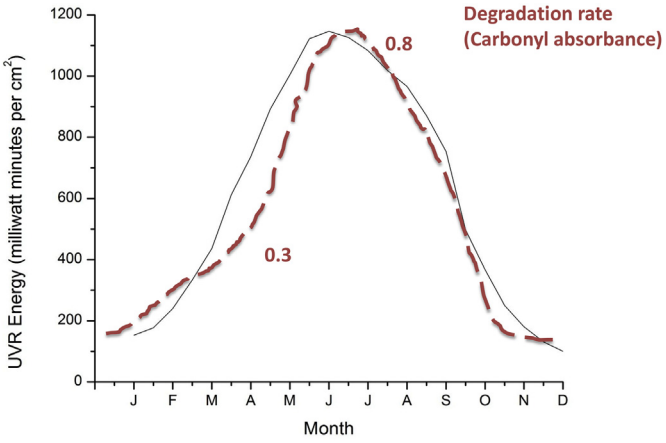

Fig. 6. UVR energy as measured over 12 months plotted along with the increase (dashed line) in carbonyl absorbance (derived from Trozzolo, 1972).

2. The fundamentals of oxidative photodegradation

The start of oxidative photodegradation is comparable to starting a fire. The "fire triangle" consists of an ignition source, fuel, and oxygen. When all 3 are present, a fire is ensured. Analogously, the "oxidative photodegradation triangle" illustrated in Fig. 5 consists of radiation exposure at a specific wavelength (UV or visible light), a material that contains a chromophore for that wavelength, and oxygen. These 3 factors combined with the absence of a sufficient antioxidant response ensure oxidative photodegradation. The energy of the radiation, time, and chromophore-specific photo-oxidation pathway determines the degree and type of oxidative photodegradation. In many typical biological scenarios, the only option to prevent degradation is to minimize or eliminate the radiation exposure.

If this does not happen, a given chemical moiety (a photosensitizer) can absorb a specific quantum of energy (E) expressed by the equation ($E = h\nu$) where h is Planck's constant and ν is the frequency of the radiation wavelength absorbed. Chemical moieties that absorb radiation, referred to as photosensitizers or chromophores, are dominated by the presence of π orbital electrons. Photon absorption in the presence of oxygen results in the formation of reactive oxygen species (ROS), chain scission, proton abstraction, and the formation of free radicals, peroxides, and carbonyl species that lead to autoxidation (Khan and Wilson, 1995; Kelen, 1983; Loan and Winslow, 1979; McKinlay and Diffey, 1987; Trozzolo, 1972; Winslow, 1977). The carbon–carbon double bonds and aromatic moieties found throughout ocular tissues are potent photosensitizers that absorb a broad range of electromagnetic radiation, leading to accelerated photodegradation (Davies and Truscott, 2001; Estey et al., 2007; Hunter et al., 2012; Parker et al., 2004; Porter, 1986; Porter et al., 1995; Pratt et al., 2011).

The link between external variation in UV energy and chemical changes to macromolecular systems has been well-established. For example, the rate of carbonyl group (simple carbon–oxygen double bonds expressed as C = O) formation upon outdoor exposure of polyethylene, a polymer initially containing only carbon and hydrogen atoms, is dependent on the time of year. Fig. 6 shows changes in ambient UV radiation energy (<313 nm) measured monthly. The energy is normally distributed throughout the year peaking around June. Fig. 6 also shows the rate of increase in carbonyl formation (which can lead to possible Norrish Type I and II reactions)[1] in weathering studies of polyethylene performed monthly in New Jersey. Note that ambient radiation and carbonyl absorbance both peak in June, showing the strong link between ambient UV and the oxidative photodegradation rate of polyethylene.

Oxidative photodegradation is an auto-oxidative process that is often described in three steps: initiation, propagation, and termination (e.g., the quenching of reactive oxygen and free radicals by an antioxidant). For example, initiation may be driven by the energy of the impinging radiation and the relative ease of abstraction of hydrogen. Allylic and tertiary hydrogen are more easily abstracted than primary hydrogen (e.g., hydrogen in polyunsaturated fatty acids (PUFAs) and at the branch points in polyethylene). If the energy of the impinging radiation ($E = h\nu$) is absorbed, then the photo-oxidative cascade can occur. UV and short visible wavelengths are capable of initiating photo-oxidation in many organic chemical bonds, including those in biological systems such as proteins and lipids.

The human retina contains a large number of endogenous photosensitizers (e.g., rhodopsin; lipofuscin). Substrates like proteins and lipids can be photooxidized through either a Type I or II mechanism (Spikes and MacKnight, 2006). Conjugated carbon–carbon double bonds and aromatic rings in lipids and proteins, respectively, absorb actinic radiation making them principle targets in photo-oxidative aging of the retina and lens.

From this view, the eye represents a paradox: it evolved to respond to light but is susceptible to light damage, and it contains structures that are nearly anaerobic (the crystalline lens) or maximally aerobic (the retina) but is susceptible to damage from oxygen. The resulting photo-oxidative cascade affects the molecules that create its very structure, primarily proteins and lipids.

3. Photo-oxidation of proteins and lipids

3.1. Proteins

Proteins comprise approximately 68% of the dry weight of cells (Davies and Truscott, 2001) and tissues and 90% of the solids content of the lens (Michael and Bron, 2011). Protein modification resulting from oxidative photodegradation occurs when aromatic side groups act as photosensitizers generating radicals via photoionization. Another major process involves oxidation of the protein via reactions with singlet oxygen generated by protein-bound or other photosensitizers (Davies and Truscott, 2001). For most proteins, direct photo-oxidation occurs when aromatic amino acid moieties absorb UV radiation. The major chromophoric amino acids containing aromatic groups are tryptophan (Trp), tyrosine (Tyr), and phenylalanine (Phe), which exhibit the highest propensity to photosensitize (Davies and Truscott, 2001; Pattison et al., 2012; Spikes and MacKnight, 2006). Fig. 7 illustrates absorption of UVB radiation for the aromatic amino acids (derived from Held (2003)). Note the strong absorption by Trp in the UV range of 250 nm–300 nm. Direct absorption of solar UV light by protein peptide bonds is negligible; however, absorption by UV-absorbing amino acid moieties can lead to the standard cascade of oxidative photodegradation. Aromatic amino acid moieties are susceptible to oxidation by singlet oxygen. Table 1 shows the relative rate of reaction of singlet oxygen with various biological molecules.

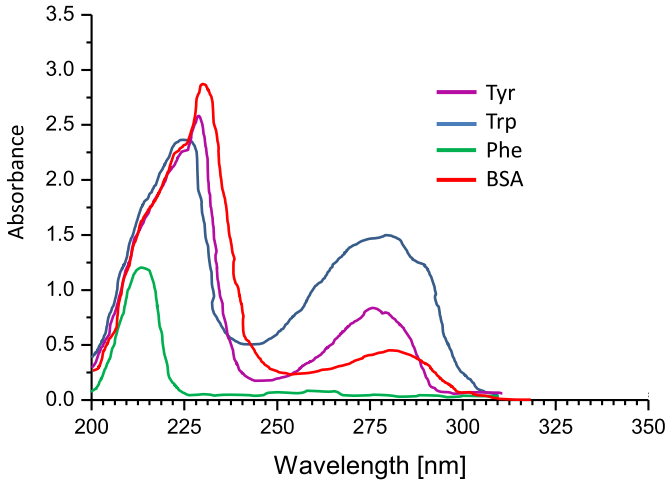

Fig. 7. Spectral Density Curves for Aromatic Amino Acids (figure redrawn from Held, 2003): Trypotophan (Trp), tyrosine (Tyr), Phenylalanine (Phe) and albumin derived from bovine serum (BSA).

[1] Norrish reactions involve photochemical reactions with ketones and aldehydes resulting from absorption of UV light (230–330 nm). Type I results in hemolytic cleavage of an aldehyde and ketone to a singlet/triplet state leading to the formation of acyl/allyl radical. Type II reactions describe the intramolecular abstraction of a hydrogen atom that results in a 1.4-biradical.

Table 1
Selected Rate Constants for reaction of Singlet Oxygen ($1O_2$) with biological target molecules (from Davies and Truscott, 2001).

Substrate	Rate constant/10^7 dm^3 mol^{-1} s^{-1}
Methyl linolenate	0.019
Methyl linoleate	0.013
Cholesterol	0.0057
2,-Deoxyguanosine	0.5
DNA	0.051
Histidine	3.2
Tryptophan	3.0
Methionine	1.6
Tyrosine	0.8
Cysteine	3.7
Ascorbate	16.0
α-tocopherol	70
β-carotene	1300
NADH	7.5
NADPH	13.4

Tryptophan exhibits a relatively high reaction rate with singlet oxygen with the polyunsaturated β-carotene exhibiting the highest reactivity in this set of examples.

3.2. Lipids

The retina contains over 50% by dry weight of lipids. Phospholipids comprise about 2/3 of these lipids and are rich in polyunsaturated (greater than two carbon–carbon double bonds) fatty acids (PUFAs). Although docosahexaenoic acid (DHA, an omega 3 fatty acid) comprises only 2%–3% of most human tissues, it is the most abundant PUFA in the retina (up to 50% (Acar et al., 2012)). Unsaturation is a key feature of common physiological lipids such as linoleates and arachidonates. The rate of reaction for peroxy lipid radicals ranges from 1 to 10^7 M^{-1} s^{-1}, with increased unsaturation a key factor in higher reaction rates (Pratt et al., 2011): the more unsaturated the lipid, the more highly oxidizable. Diene lipids such as linoleic and arachidonic acid and the highly conjugated DHA undergo autoxidation more readily than monounsaturated lipids such as oleic acid or cholesteryl oleate. Although unsaturated lipids have many optimal qualities (e.g., fluidity) when compared to saturated lipids, their high susceptibility to autoxidation requires significant antioxidant protection.

Light exposure and the broad absorption spectra of PUFA make the retina particularly susceptible to lipid peroxidation. Lipid peroxidation is a process in which molecular oxygen and lipid react by a free radical chain sequence (the chain is propagated by lipid peroxyl radicals abstracting a hydrogen from another lipid and so on). The product of this auto-oxidation tends to be lipid hydroperoxides. These intermediary products have been strongly linked to the more deleterious aspects of aging and retinal disease (Anderson et al., 1984; Miquel et al., 1998; Tang et al., 2013). Supplementation with antioxidants like lutein (which, for example, co-localizes with DHA in retinal membranes) directly reduces circulating lipid hydroperoxides even when given to premature infants (Perrone et al., 2010).

Although lipid peroxidation can occur in the absence of electromagnetic radiation, it can be accelerated when PUFA moieties absorb radiation. The absorption intensity and wavelength dependence is dictated by the number of conjugated double bonds. There are both classic high rate autoxidation as well as photo-oxidation of unsaturated fatty acid moieties in lipids.

4. Ocular phototoxicity in the cornea, lens, and retina

Light is the fundamental stimulus for vision. Visible (and a small amount of UV ~1%) radiation is absorbed in the adult retina by cone photopigments and rhodopsin (where 1,1 cis-retinaldehyde is converted to 1,1 trans-retinaldehyde). At a young age, greater amounts of UV radiation reach the retina (Merriam, 1996; Gaillard et al., 2011). Transducing light is the basis of all subsequent visual processing (Wald, 1945; Tang et al., 2013). The reconversion to 1,1 cis-retinaldehyde in the RPE completes the visual cycle. The steps in this reconversion are the subject of basic research to understand retinal degeneration. Several retinal diseases are associated with malfunction at specific steps of the visual cycle (Stone, 2007; Tang et al., 2013). Although the eye is an organ adapted to respond to light, it can be damaged by excessive exposure (Glickman, 2011; Hunter et al., 2012). The specific manner in which such exposure influences the major components of the eye is defined by their essential structure.

Table 2
Corneal responses to excessive ultraviolet radiation (from Cullen, 2002).

Acute response	Chronic response
Photokeratitis	Climate droplet keratopathy
Damage to epithelium, endothelium, keratocytes	Pterygium
Transient haze and swelling	Possible endothelial dystrophy
Opacification	Cancer in some nonhuman species

4.1. Cornea

The corneal epithelium makes up approximately 10% of the cornea but absorbs UV light strongly due to its high protein and nucleic acid content. The cornea responds both acutely and chronically to UV radiation, as outlined in Table 2 (Cullen, 2002; Pitts and Tredici, 1971; Zuclich, 1989). The transmission and absorption spectra for the cornea are shown in Figs. 8 and 9, respectively.

One useful approach to evaluating the potential for light to damage ocular structures is the examination of action spectra. Action spectra consist of graphs that plot the rate of physiological activity (or threshold radiation dose) versus wavelength and provide a quantitative view of radiation-induced ocular phototoxicity. Cullen (2002) collected action spectra for damage to the cornea and conjunctiva; these are plotted together in Fig. 10. In this graph, the *y* axis represents the threshold value for damage to occur. *In vivo* responses to overexposure to UV radiation (Chao et al., 2013) include haze in the epithelium and stroma, discharge and debris in the tears, and granules in the endothelium.

Mounting evidence supports the role of the corneal crystallin aldehyde dehydrogenase (ALDH) 3A1 (3A1) as an important factor in protecting the cornea from oxidative photodegradation. 3A1 comprises approximately 5%–50% of soluble proteins in mammalian cornea. 3A1 protects against UV-induced oxidative stress via metabolism of toxic aldehydes, generation of reduced nicotinamide-adenine dinucleotide phosphate (NADPH), direct absorption of UV light, scavenging of ROS and chaperone-like activity (Estey et al., 2007). Chaperone protein roles have also been elucidated in the lens and the brain (Andley, 2009; Andley et al., 2014; Bron et al., 2000; Shao et al., 2013; Truscott, 2009).

Corneal overexposure to UV radiation results in photokeratitis and has been referred to as “snow blindness,” “arc eye,” and “welder's flash.” Symptoms occur several hours after overexposure, with the time delay inversely proportional to exposure time. Epithelial damage produces a gritty feeling, photophobia, and tearing. Severe exposure results in haze and loss of vision. Higher exposures result in epithelium exfoliation, excruciating pain and blepharospasms (blinking uncontrollably). Symptoms usually abate

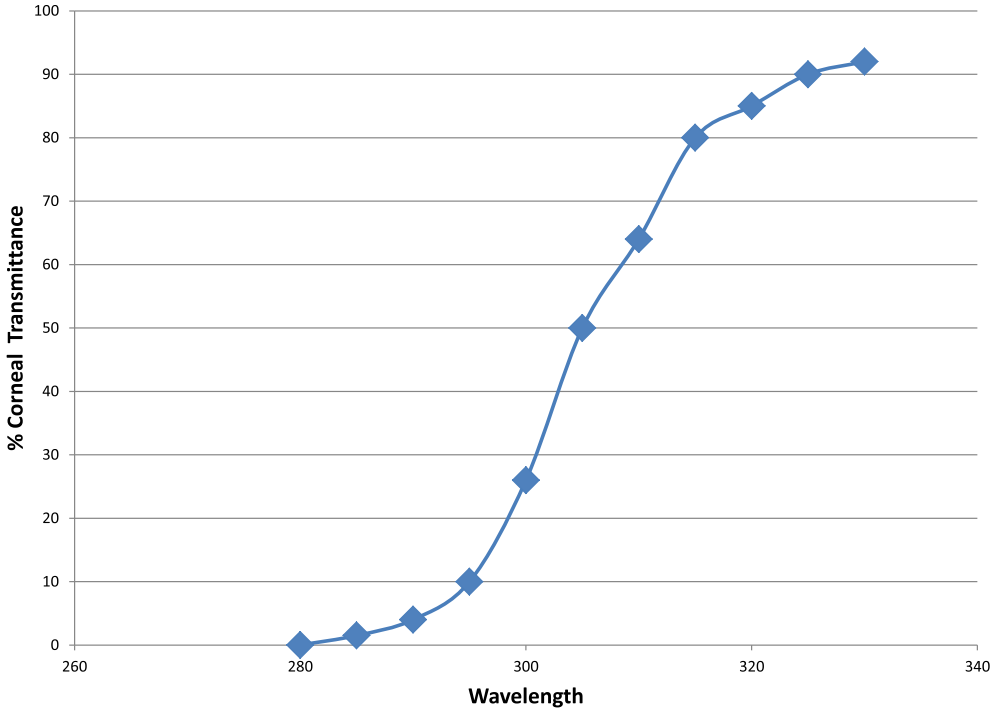

Fig. 8. Transmittance spectrum of the cornea (Cullen, 2002).

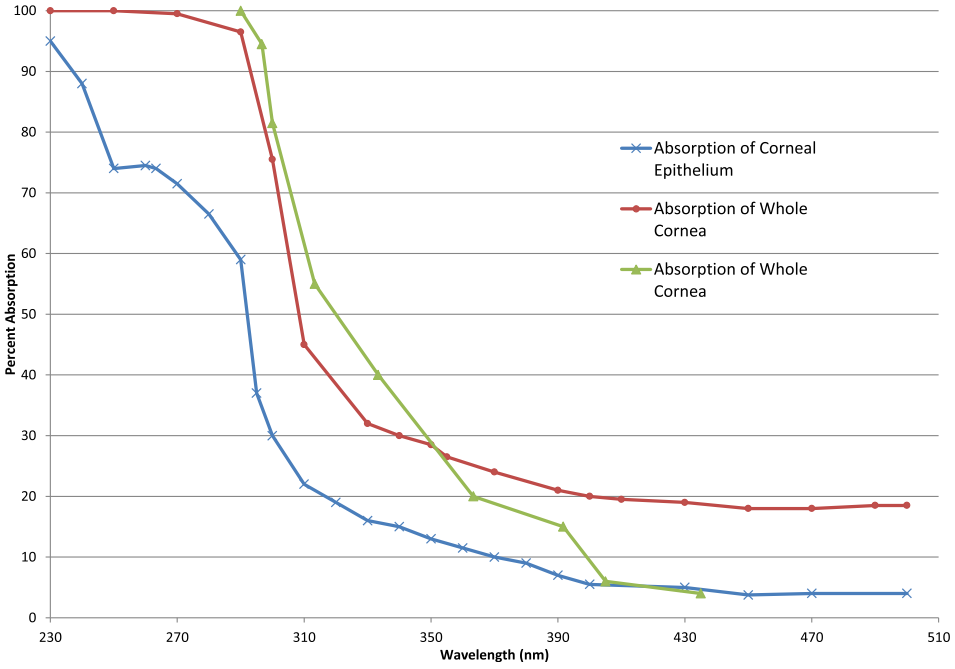

Fig. 9. Absorption of UVR by the epithelium and the cornea from 2 sources (derived from Pitts and Tredici, 1971).

within 2 days. The primary response is in the corneal epithelium, but effects can penetrate beyond Bowman's membrane to the stroma (Cullen, 2002). Pterygium is a chronic response to UV radiation exposure (Chao et al., 2013). It is an inflammatory, proliferative growth on the cornea and conjunctiva that can impair vision. Chronic UV exposure leads to formation of abnormal fibroblasts and mutations in basal epithelial cells (Norval, 2011). The predominance of pterygium on the nasal side is most probably a result of the sun's rays passing laterally through the cornea, where it undergoes refraction and becomes focused on the limbic area. Reflected UV plays a greater role than direct sunlight (Sliney, 2011).

Photokeratitis and pterygium are two eye diseases where UV-induced altered immune response plays a central role. The mechanisms involved in these adverse events include oxidative stress, DNA damage, and necrotic receptor activation that lead to apoptotic cell death. *In vitro* studies have demonstrated that UV irradiation of

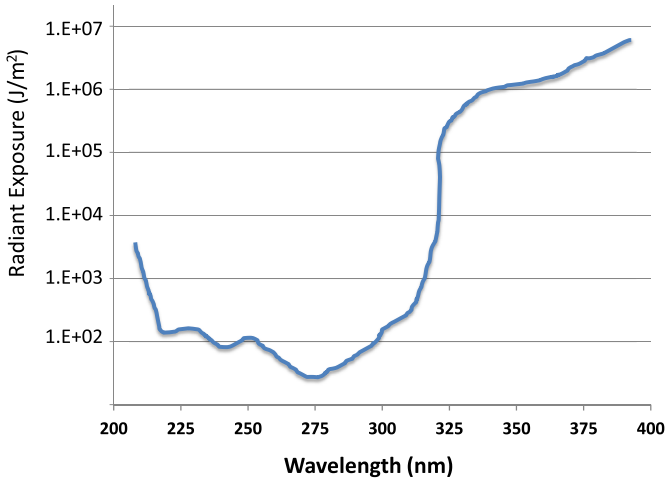

Fig. 10. Action Spectra of Corneal and Conjunctiva UV radiation exposure (the average line is based on individuals curves from Cullen, 2012).

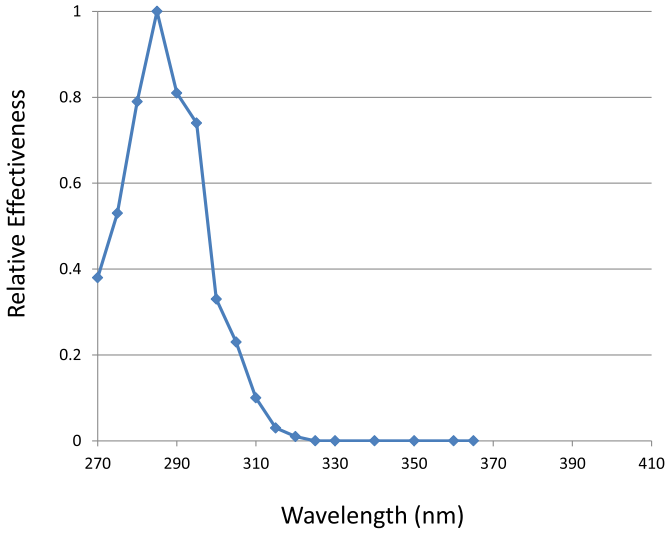

Fig. 11. The action spectrum for cataract formation (derived from Lucas, 2011).

corneal stromal cells induces the production of pro-inflammatory cytokines. Additionally, UV radiation generates ROS, known to also generate pro-inflammatory cytokines. Pterygium can lead to the release of enzymes that cause the production of growth factors such as vascular endothelial growth factor (VEGF), a key step toward neovascularization (Norval, 2011).

4.2. Lens

An action spectrum for cataract formation is shown in Fig. 11 (Lucas, 2011). This curve is nearly identical to the action spectrum for lens proteins. This similarity is due to absorption of UV radiation by the aromatic amino acid moieties Trp, Tyr, and Phe present in lens proteins.

The crystalline lens is composed of proteins known as crystallins that make up 90% of its solid content. These include alpha, beta, and gamma crystallins, of which the alpha crystallins have the highest molecular weight and are in the highest concentration. Alpha crystallins, which are in the “chaperone” or “heat shock” family of proteins, have a protective role in preventing the aggregation of the beta and gamma proteins. The beta and gamma proteins' key functions are transparency and structure (Bron et al., 2000).

Other lens components include the capsule, gap junctions, differentiated and mature fiber cells, and epithelial cells. The capsule is the collagenous shell of the lens. The gap junctions consist mainly of intercellular protein channels (connexins and aquaporins) critical for the transfer of aqueous salts, antioxidants, etc. (Mathias et al., 2010). The lens also maintains homeostasis via solute exchange with the vitreous and aqueous (Dahm et al., 2011). The nucleated, metabolically active epithelial cells are located on the anterior half of the elliptical lens and produce critical nutrients (e.g., the antioxidant glutathione [GSH]), that diffuse through the lens. With age, solute diffusion is hindered in the lens nucleus (Sweeney and Truscott, 1998). Epithelial cells lose their organelles and differentiate into lens fiber cells with time (hence achieving the relative transparency necessary for the transmission of light). The water content of the nucleus and cortex are 63% and 69%, respectively. The water content does not change with age in either region of the lens (Fisher and Pettet, 1973).

The proteins in the nucleus of the lens are the same age as their human host (the only tissue in the body that does not undergo biological renewal). Therefore, the nuclear proteins are unique in that they experience literally a lifetime of exposure to electromagnetic radiation.

Fig. 12 illustrates that the loss of soluble alpha crystallin proteins concomitant with an increase in lens modulus accelerates after the age of 40. This provides evidence that precipitation or denaturing of lens proteins is a major factor in presbyopia and is now considered a precursor to cataracts (Bron et al., 2000; Truscott, 2009).

Lens proteins become progressively modified at Trp amino acid sites, with the number of modifications increasing with age (Dillon and Atherton, 1990). 3-OH Kynurenine is protective. With age, however, kynurenine, a significant by-product of lens protein photo-oxidation at Trp sties, becomes damaging. This is because of the tendency to undergo deamination at physiological pH, with the resulting reaction products which covalently bind to other proteins. Xanthurenic acid is also formed with age and is also photosensitizing (Roberts et al., 2001). These 3-OH-kynurenine-modified proteins become susceptible to wavelengths of light that penetrate the cornea (Davies and Truscott, 2001; Pattison et al., 2012; Spikes and MacKnight, 2006). Kynurenine-based chemistries absorb a broader range of radiation, resulting in accelerated oxidative damage through a singlet oxygen photooxidative mechanism (Balasubramanian, 2000; Roberts et al., 2000; Davies and Truscott, 2001).

Upon exposure to wavelengths from 305 to 385 nm, bovine lens proteins accumulated hydrogen peroxide and protein-bound peroxides, which increased with time and when exposed to shorter wavelengths. Peroxide formation was accompanied by an increase in Tyr- and Phe-derived products, known to be elevated in human cataract lens proteins. This provides one mechanistic explanation for UV light–mediated protein oxidation in cataract lenses (Parker et al., 2004). There is likely, however, more than one mechanism. It has also been shown, for instance, that both kynuenine (Balasubramanian, 2000) and xanthurenic acid (Roberts et al., 2001) produce singlet oxygen which then photooxidizes lens proteins leading to the formation of cataracts.

In summary, photooxidation of lenticular chromophores increases with age due to:

- Liquefaction of the vitreous, increasing oxygen concentration in the lens (Beebe et al., 2011; McLaren et al., 1998)
- Impediment of antioxidant diffusion in the lens (Sweeney and Truscott, 1998)

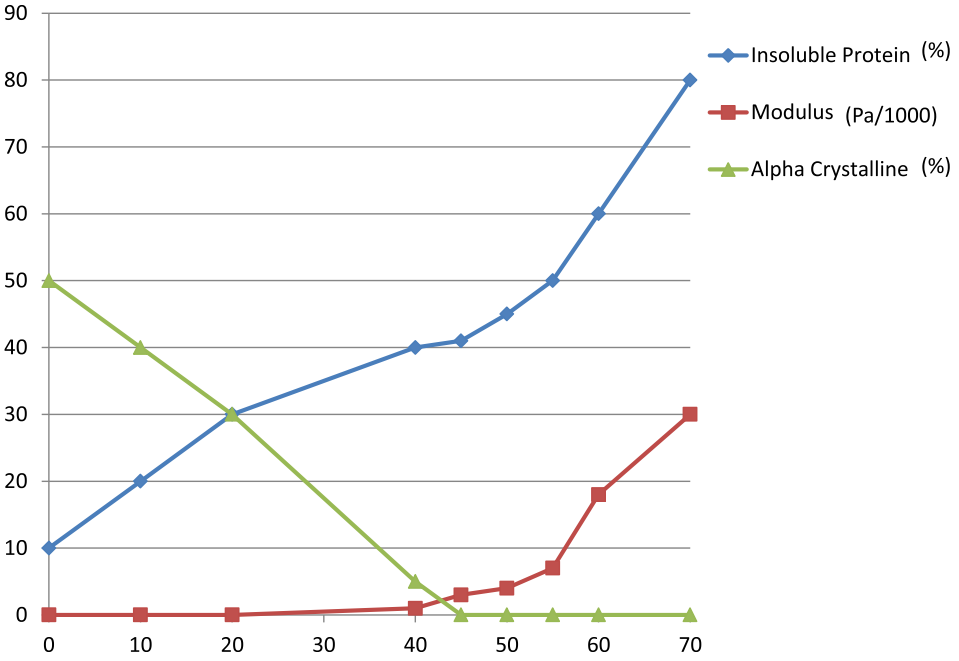

Fig. 12. Alpha crystallins, Insoluble proteins, and increasing modulus with age (derived from Truscott, 2000).

- Reduction in key enzymes that maintain antioxidant levels (Fecondo and Augusteyn, 1983)
- Increased level of chromophores (Davies and Truscott, 2001; Roberts, 2001)

4.3. Retina

Although predominately visible light reaches the retina, a small (~1%) amount of UV radiation does actually penetrate to the adult retina (Weale, 1988; van de Kraats and van Norren, 2007a).[2] Werner and Spillmann (1989) described the very negative effects of UV radiation on the retina. The first intraocular implants (regular use of which started in the 1970s) were made of polymethylmethacrylate (PMMA) and, unlike the natural lens and later intraocular lenses (IOLs), did not include UV-absorbing chromophores. Werner studied patients who had undergone bilateral IOL implantation, but with UV-chromophores in only one eye (the other IOL transmitted light from 300 to 400 nm). S-Cone sensitivity was measured in both eyes after 5 years and is shown in Fig. 13. As seen in this figure, the eye that lacked the UV block displayed dramatic and selective loss of S-cone sensitivity compared to the contralateral eye that was protected.

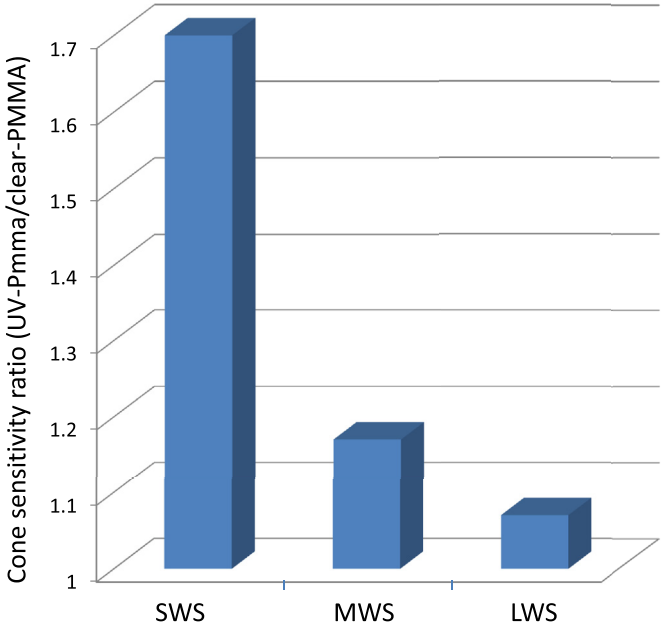

Fig. 13. Average sensitivity across wavelengths for eyes with a UV relative to a clear IOL. The experimental methods allowed isolation of the s-cone (SWS), M-cone (MWS) and L-cone (LWS) systems. Data derived from Werner and Spillmann (1989).

UVA and short visible wavelengths produce similar phototoxic effects in the retina. Since the cornea and lens focus light on the retina, a collimated beam of light on the cornea results in up to five orders of magnitude higher energy on the resultant foci at the retina. Energy is inversely proportional to wavelength, but the resulting biological damage is not linear, as shown in Fig. 14. For example, visible blue light is much more damaging than visible green since it has sufficient energy to initiate oxidative reactions. Longer wavelengths can damage the retina but do so via thermal mechanisms. Fig. 15, compiled via a meta-analysis (Glickman, 2011), illustrates the action spectrum for retinal damage via exposure to electromagnetic radiation in the UV/blue light region (see also van Norren and Gorgels, 2011). The chromophore is the bleach product of rhodopsin.

The rhodopsin bleach product (a critical chromophore for UV-based degradation) is rhodopsin after light activation (i.e., opsin now attached to 1, 1 trans-retinaldehyde). Other prospective chromophores in the retina and RPE that can absorb above wavelengths of 360 nm include photoreceptor pigments, the RPE pigments melanin, lipofuscin, and melanolipofuscin granules and a condensation product of two 1, 1 trans-retinaldehyde molecules

[2] This can lead, for instance, to retinal lesions that are caused by exposure to helium–cadmium lasers which contain UV (Schmidt and Zuclich, 1980).

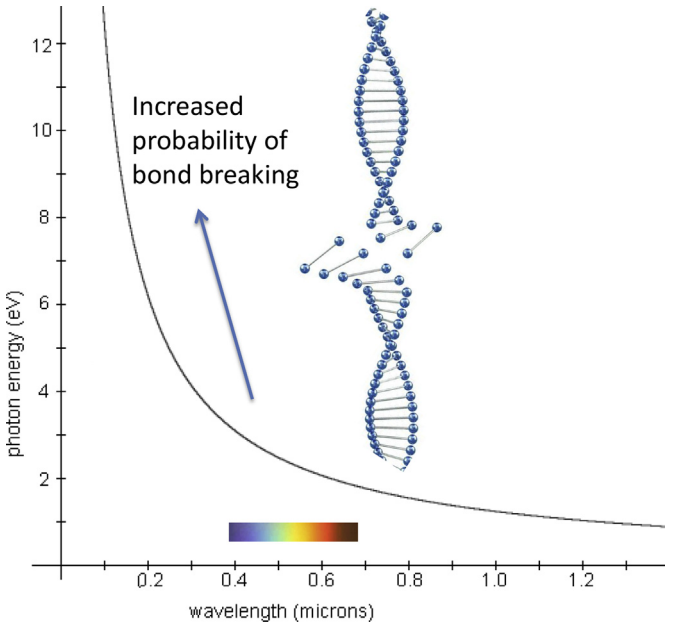

Fig. 14. Photon energy as a function of wavelength.

with a molecule of phosphatidylethanolamine, abbreviated as A2E (Roberts et al., 2002; Wielgus and Roberts, 2012).

Lipofuscin is formed in the RPE cells and is largely based on oxidative photodegradation of shed photoreceptor outer discs. The degradation products are predominately a mixture of lipids and proteins. RPE pigment granules are photosensitizers and can participate in the oxidative photodegradation cascade. Since lipofuscin itself is a photo sensitizer, accumulating lipofuscin will cause a cascade that produces more lipofuscin. Elevated lipofuscin levels have been associated with AMD and the fact that damage to the retina appears to accelerate with age (Hammond et al., 1998; Ablonczy et al., 2013, 2014; Hunter et al., 2012).

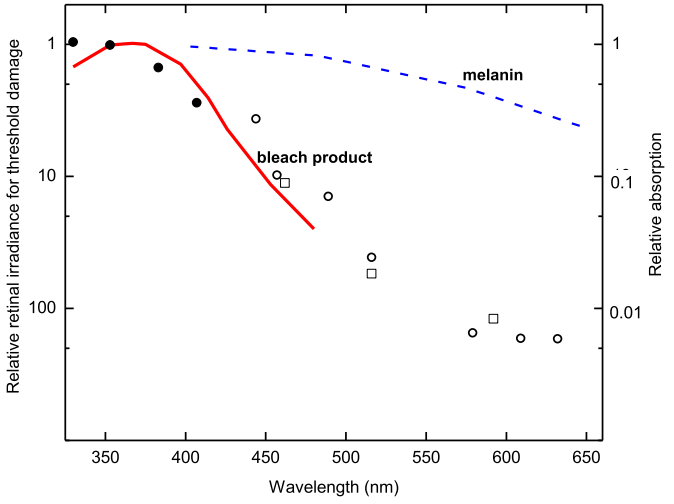

Fig. 15. Damage threshold for UVA/Blue Light in the Retina. Solid line is absorption spectrum of rhodopsin bleach product and individual data points are damage thresholds. (Derived from Glickman, 2011).

5. Preventing ocular photodegradation through endogenous and exogenous filters

For synthetic and natural polymers, shielding from harmful radiation is achieved in the most direct fashion through the simple use of filters: opaque surface coatings, staying indoors, wearing a wide brimmed hat, etc. The ocular media progressively filters light through the cornea, aqueous, lens, and vitreous, respectively, ending with high-end UVA and the full visible spectrum irradiating the retina. There appears to be no useful function for UV radiation in the ocular system with the possible exceptions of lenticular yellowing paradoxically protecting the retina from damaging short-wave light (Dillon and Atherton, 1990) and a possible role of UV radiation in slowing myopia progression (Sherwin et al., 2012). Filtering all UV radiation at the cornea is a sound approach for minimizing photo-oxidation in ocular media (Roberts, 2011). Similarly, filtering short-wave visible light is widely touted as a means of minimizing damage due to the blue-light hazard (Algvere et al., 2006). Visible light, of course, is just a very small portion of the electromagnetic spectrum. Humans perceive the portion of the electromagnetic spectrum from about 400 nm to 700 nm (a billionth of a meter). Such light is not equally capable, however, of damaging retinal/RPE tissue.[3] This is because the energy of light is inversely proportional to its wavelength: longer wavelengths are less energetic than shorter wavelengths. As applied to the eye, light from about 500 nm to 700 nm can damage the retina, but only through thermal mechanisms (although it can increase the potential that shorter-wavelengths will be damaging because it raised the overall energy state). An enormous amount of light would be necessary to heat the retina enough to cause damage (heat is largely dissipated by the RPE and choroidal vasculature).

Empirical evaluations (mostly using animal models; e.g., Barker et al., 2011) have shown that light from about 400 to 500 nm is the most damaging to retinal tissue (Algvere et al., 2006) because (1) it reaches the retina and is not significantly absorbed by anterior structures, (2) it still retains enough energy to initiate photochemical damage (e.g., convert inert oxygen into reactive forms), and (3) it fits the action spectrum of retinal photosensitizers (Margrain et al., 2004).

5.1. Short-wave absorption by the retinal macular carotenoids

Before visible light can be processed by the retinal photoreceptors, it must pass through two significant endogenous filters: the crystalline lens (progressively yellowed over time by oxidation) and the inert pigments in the inner retina, often referred to as macular pigments. These screening pigments are found in the inner retina distal to the outer segments of the cones (and a relatively small proportion of rods). Along with the fovea's characteristic anatomy, these yellow pigments are one of the central retina's most obvious features and are responsible for the term macula lutea, which is used clinically to designate this retinal region. The Nobel Laureate George Wald (1945) was the first to identify that the pigments were xanthophyllic carotenoids derived from the diet. Approximately 40 years later, Bone et al. (1985) definitively identified these macular pigments as the specific xanthophylls (3R,3′R,6′R)-lutein (L) and (3R,3′R)-zeaxanthin (Z). This same group

[3] Another common distinction is to characterize light damage to the retina/RPE as Type I and II (Kremers and Van Norren, 1988). Type I occurs at lower light levels and is largely mediated by receptoral photopigment (based on the similarity of the actinic action spectrum to the absorption spectrum of photopigment). Type II tends to occur at higher levels (but much lower than photocoagulation) and is mediated at the level of the RPE.

(Bone et al., 1993) later identified a stereoisomer they termed (3R,3′S)-mesozeaxanthin (MZ). L, Z and MZ form the macular pigments. Because the macular pigments are in the inner retinal layers, they screen photoreceptors in and around the fovea (they peak sharply in the very center of the macula [i.e., the fovea] and decline rapidly with eccentricity (Bone et al., 1993; Hammond et al., 1997)). The optical density (OD) of these pigments in the human retina varies widely; individuals have been identified with densities that are optically undetectable to as high as 1.6 at peak absorption (460 nm). Such large differences, especially when considered over decades of life (pigment density tends to be temporally stable (Hammond et al., 1997)), result in equally large differences in the exposure of the macular receptors to actinic short-wave light. An empirical study of monkeys has shown that macular pigments directly protect the retina from imposed light damage due to high-energy lasers (e.g., (Barker et al., 2011)). These acute studies are consistent with the putative role of the pigments in protecting the vulnerable lipid-rich photoreceptors from the actinic effects of blue light and empirical data on their role in preventing age-related cataract and macular degeneration (Hammond and Lien, 2013).

The spectral density curves for L and Z in both aggregated and monomeric forms are shown in Fig. 16 (Sujak et al., 2000). Note the broad range of absorbance from less than 350 nm to approximately 550 nm. The aggregated forms are much more absorptive in the UVA region of the electromagnetic spectrum.

5.2. Short-wave absorption by the yellowing crystalline lens

The lens and cornea are the most transparent tissues within the body. Most cells, even those that are avascular (e.g., bone cells), are

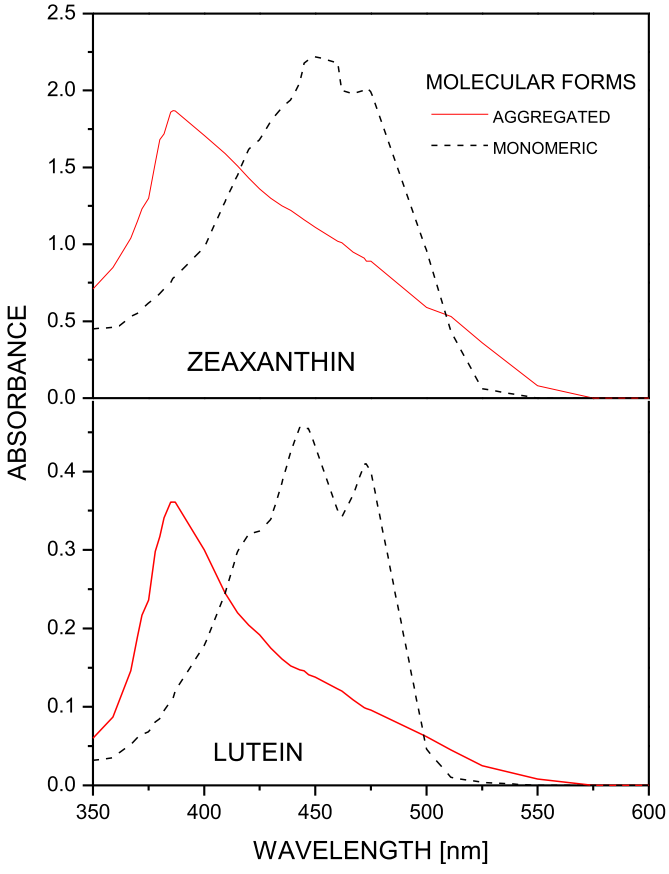

Fig. 16. Absorption Spectra for Monomeric and Aggregated forms of Lutein and Zeaxanthin (derived from Sujak et al., 2000).

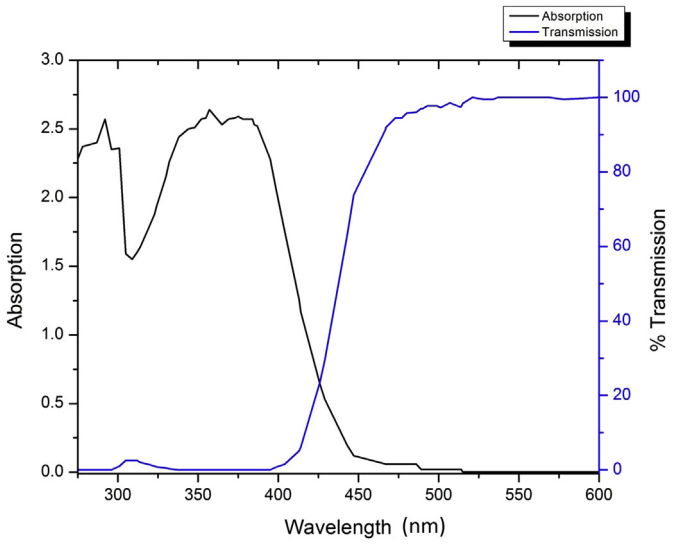

Fig. 17. The absorption/transmission characteristics of the neonatal lens (derived from Gaillard et al., 2011). Note the increased transmission centered around 320 nm (this "window" closes in the teen years).

opaque due to their organelles, other absorbing chromophores, and high optical scatter arising from an uneven distribution of refractive elements. In contrast, the young lens has nearly no light-absorbing pigments, and the packing of the layers of clear crystallin cells is highly ordered. Controlled apoptosis during development removes optically dense organelles, leaving the cell essentially alive but without the ability to regenerate or repair damage. As such, any damage to fiber cells within the lens simply accumulates with age, causing the lens to slowly opacify. Transamidation, methylation, and oxidation account for the major post-translational modifications of lens proteins (Andley et al., 2011; Beebe et al., 2011; Michael and Bron, 2011; Sweeney and Truscott, 1998; Truscott et al., 2012; Lampi et al., 2014). This opacification is both distinctive and relatively stable across the lifespan. It is well known, for instance, that lens absorbance is strongly related to wavelength (Wyszecki and Stiles, 1982). Another important feature of lens OD is that absorption increases linearly with age and that individual variation is large (Werner, 1982). The lens is most transparent in infancy (Gaillard et al., 2011). Indeed, the increased transparency of the crystalline lens to UV in childhood has been argued as a major reason that the retina appears to rapidly age during that period (e.g., as evidenced by the rapid buildup of lipofuscin). The crystalline lens (see Fig. 17) has a small window of transparency around 320 nm that does not fully close until teen years (Gaillard et al., 2011). It is worth noting that the absorbance of L and Z in their aggregated forms is shifted toward this portion of the UV spectrum. Hence, if a significant portion of tissue L and Z is in aggregate form in the young retina (which is probably the case), it is likely that this provides additional protection against actinic damage to the retina early in life.

Ironically, older retinas are more protected by the crystalline lens by virtue of its damage: as the lens ages and oxidizes, it progressively yellows (and OD increases) and absorbs higher amounts of UV and visible short-wave light (Werner, 1982). It is important to note that not all older lenses offer this increased protection from short-wave visible light. Although the OD of the lens increases in some older individuals, it does not increase in all. Indeed, cataractous lenses can sometimes be quite transparent to visible light (due to, for instance, off-optical axis location of the cataract). For example, Sample et al. (Sample et al., 1989) measured lens OD at 410 nm in 84 subjects (18–78 years of age) with intact lenses and

with clinical diagnosed cataracts. She found that lens optical density (OD) increased from around 0.30 for subjects in their 20s (ranging from 0 to ~0.4) to about 1.4 for subjects in their 70s (ranging from ~0.1 to ~2.5). On average, elderly subjects with cataracts had higher OD than subjects without cataracts. In both cases, though, there were a substantial number of elderly individuals with very transparent lenses (one cataractous patient, for example, had an OD near zero). Such a finding makes sense. OD is determined by a variety of factors, including the concentration of the absorbing chromophore (e.g., oxidation causing protein aggregates), light scatter, and path length. These factors do not change in tandem (Pokorny et al., 1987) or in the same way across individuals.

5.3. UV and short-wave absorption by intraocular implants

The first artificial lens (using PMMA) was implanted at St. Thomas hospital in London in 1949. Regular use of IOLs, however, did not occur until the 1970s with the use of silicone and acrylic lenses (Kohnen, 2009). Modern IOLs incorporate UV-absorbing chromophores, but not all commercially available lenses are equally effective in absorbing UV light (Werner and Spillmann, 1989; van de Kraats and van Norren, 2007b). For example, the Regent glass IOL absorbed only up to about 334 nm, whereas the Polylite polycarbonate absorbed up to 387 nm. A relatively recent approach in IOLs is to add a yellow dye to the substrate (so called blue-blocking IOLs introduced in the 1990s). For example, the design of the Acrysof Natural IOL (Ernest, 2004) is intended to mimic the UV-and-short-wave absorbing qualities of an adult 53-year-old natural lens. Sparrow et al. (2004) have shown that blue-absorbing IOLs can reduce light-initiated cell death in cultured RPE cells (laden with the lipofuscin photosensitizer A2E). Rezai et al. (2008) found a similar protective effect when measuring the light-induced apoptosis of RPE cells. Although Mainster and Turner (2001) have argued that blue-blocking IOLs may interfere with the circadian response, recent reviews of the extant literature (Henderson and Grimes, 2010; Yang and Afshari, 2014) indicate that any effects of blue-blocking IOLs on visual acuity/contrast sensitivity, scotopic sensitivity, color perception, or circadian rhythms was minimal and clinically insignificant.

5.4. UV and short-wave light absorption by spectacle and contact lenses

Although most spectacles and sunglasses have UV-blocking characteristics, like IOLs, this is by no means uniform. For example, Lin et al. (Lin et al., 2002) measured numerous spectacle lenses and found widely varying UV absorption. Indeed, some sunglasses, by darkening the visual field and causing pupil dilation, can actually increase UV transmission into the eye (Pitts and Tredici, 1971; Sliney, 2011). A spectrophotometric study (Velpandian et al., 2005) of 20 lenses (11 hard resin and 9 glass) showed that 75% of these lenses failed to provide the 95% UVA protection recommended by the U.S. Food and Drug Administration (FDA; the FDA class II blocker as described at http://www.aoa.org/x12724.xml). Neither brand nor price seems to predict the quality of UV protection available in sunglasses (Carnevale et al., 2012). One clear disadvantage of lenses worn in front of the eye is that they often do not block light coming in from the sides.

UV blocking contact lenses that completely cover the pupil and limbus, help to prevent the UV oblique rays from reaching the lens. Early contact lenses, although uniformly absorbing UVB, were quite variable with respect to UVA (only 2 out of 9 tested, for example, had significant UVA absorption in a study done in 1999 (Anstey et al., 1999)). In the last decade, the UV-blocking characteristics of contact lenses have improved. Fig. 18 presents the results for spectral transmission curves of select worn versus unworn contact lenses. Note that the Acuvue® Advance® lenses exhibit enhanced UV-filtering capability up to 390 nm. The worn Acuvue® Advance® lenses demonstrated some additional mild light filtering in the visual region of the spectrum, attributed to tear fluid component deposition (Lira et al., 2009). Fig. 19a through 19c plots the UV absorption of three commercial contact lenses; Acuvue® 2®, Acuvue® Advance®, and Acuvue® Oasys® (John Enns 2003; personal communication). These lenses absorb practically all UVB radiation and a major portion of the UVA spectrum. The Oasys lens is the most efficient UV absorber of the three Acuvue lenses.

"A good UV absorber should strongly absorb in the 300–400 nm wavelength range, though, ideally, none at all in the visible range in order to prevent any unwanted coloration. Numerous investigations have been reported on the deactivation mechanism of intramolecularly hydrogen-bridged UV absorbers. It has been established that photoexcitation of these compounds is followed by an excited-state intramolecular proton transfer (ESIPT) and subsequent rapid, mainly radiationless deactivation, including a proton back-transfer to the original S_0 ground state. This process constitutes a classic intramolecular Förster Cycle and ensures that the absorbed ultraviolet radiation is rapidly transformed into vibrational energy. This is essential for the high photostability required from an efficient UV absorber" (Waiblinger et al., 1999).

Animal models have shown that UV-blocking contact lenses can directly reduce UV-induced oxidative damage to the cornea, aqueous, lens (Chandler et al., 2010) and retina (Ibrahim et al., 2012). A number of organizations (e.g., the American Optometric Association) and comprehensive reviews (Chandler, 2011; Walsh and Bergmanson, 2011) have endorsed the use of UV-blocking contact lenses covering the limbus as greatly reducing the potentially toxic effect of light-induced oxidative damage to the eye.

6. Prevention of ocular photodegradation through endogenous and exogenous antioxidants

Oxidative stress is a common phenomenon in living systems. It is defined as an imbalance between ROS and antioxidants.

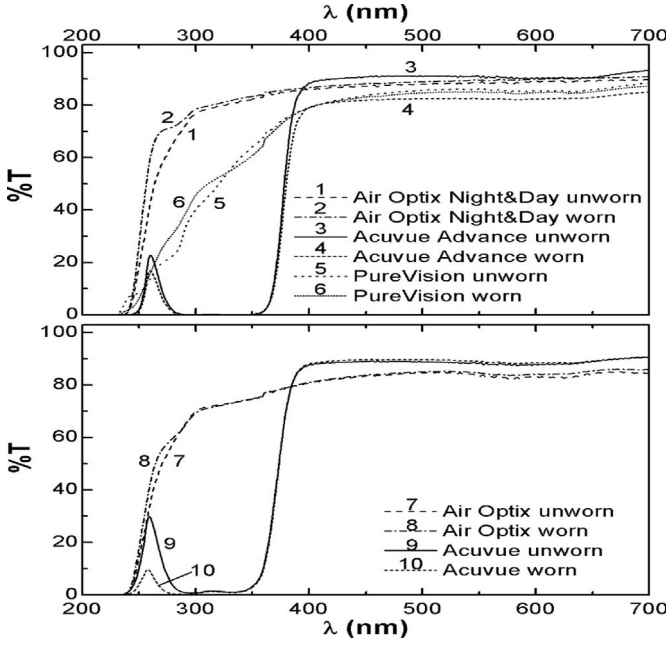

Fig. 18. Spectral transmittance of representative contact lens products (Lira et al., 2009).

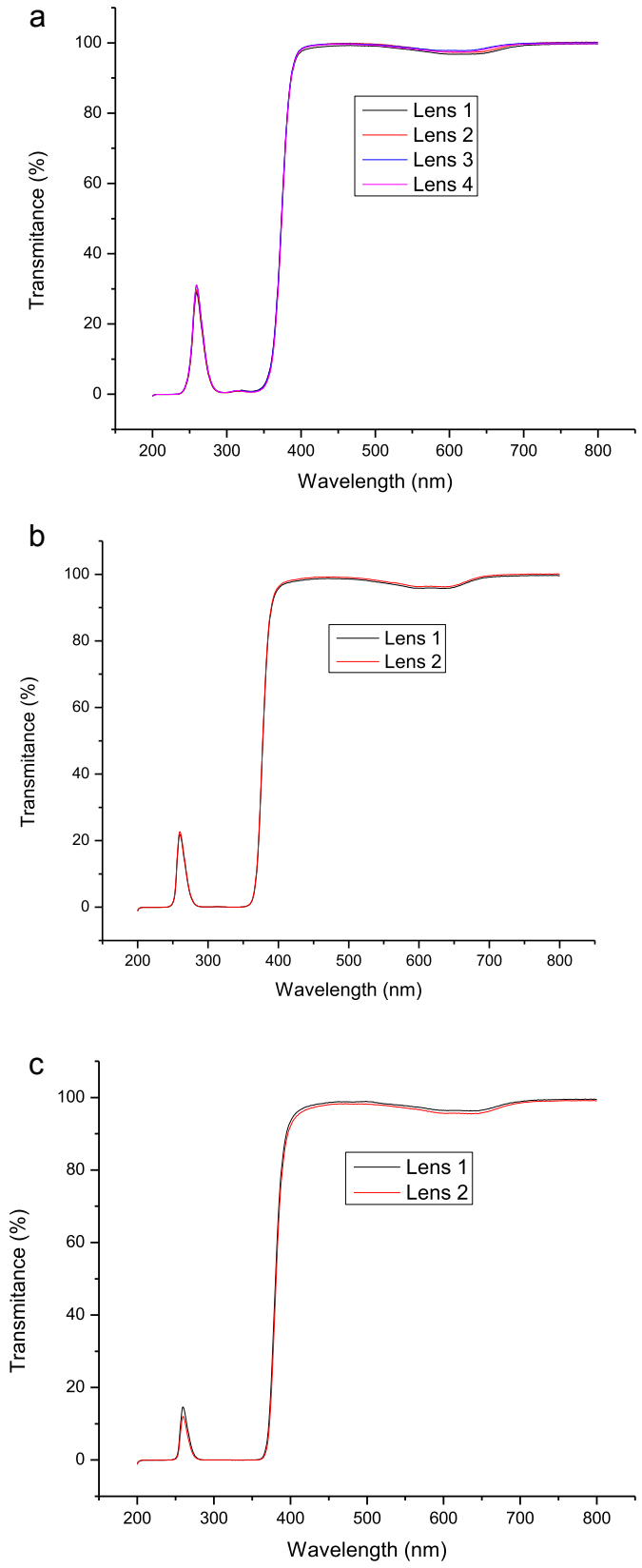

Fig. 19. a. Spectral Density Curve of Acuvue 2 (etafilcon) Enns, John (2003, Personal communication). b. Spectral Density Curve of Acuvue® Advance® (galyfilcon). c. Spectral Density Curve of Acuvue® Oasys® (senofilcon).

Disturbances in the normal redox state of cells can cause toxic effects through the production of peroxides and free radicals that damage all components of the cell, including proteins, lipids, and DNA. Studies in the protection of synthetic polymers from oxidative photodegradation offer great insight into understanding biological systems.

Interception of oxidative pathways is often achieved via radical scavengers such as aromatic hindered phenols that result in non-propagating radicals. The hydrogen atom in the alcohol group is easily abstracted, leaving a resonance stabilized free radical. This general structure and mechanism applies to many materials referred to as antioxidants. An antioxidant is a molecule that inhibits the oxidation of other molecules. Oxidation is a chemical reaction that transfers electrons or hydrogen from a substance to an oxidizing agent. Oxidation reactions can produce free radicals. In turn, these radicals can start chain reactions. When the chain reaction occurs in a cell, it can cause damage or death to the cell. Antioxidants terminate these chain reactions by removing free radical intermediates and inhibit other oxidation reactions. They do this by being oxidized themselves, so antioxidants are often reducing agents such as thiols (GSH and L-cysteine), ascorbic acid (vitamin C), hindered phenols (α–tocopherol) or polyphenols.

The lens, for example, utilizes a number of antioxidant enzymes including: superoxide dismutase; catalase; glutathione reductase; and glutathione peroxidase (GPX-1). These are likely (Gao et al., 2011) the primary defense against protein aggregation (and cataracts), with the chaperone alpha crystallins as the secondary defense. This conclusion is supported by findings in mice.

In addition to antioxidant enzymes, dietary antioxidants likely also protect the lens. In addition to antioxidant enzymes, dietary antioxidants likely also protect the lens (e.g. lutein (L), zeaxanthin (Z) and tocopherols). Yeum et al. (1995) has suggested, for example, has suggested the possibility that these phytochemicals, classically thought to mostly protect the retina, could also prevent lipid peroxidation and resulting opacification of the lens. *In vitro* studies of incubation of human lens epithelial cells (HLECs) in L, Z, and α–tocopherol resulted in reduced oxidative damage. Pre-incubation dramatically reduced the levels of hydrogen peroxide-induced protein and lipid peroxidation, and DNA damage in HLECs. Most, but not all, epidemiological studies have supported a role for L and Z in the prevention of cataract (see the recent review by Vishwanathan et al., 2013). The strongest link appears to be with nuclear cataract, and to a lesser degree, posterior subcapsular cataract (with little or no association to cortical cataract).

Incidence of age-related nuclear cataracts is reduced with higher serum levels of L and Z (antioxidants and light filters (Karppi et al., 2012)). The reduced antioxidant capacity in the lens combined with evidence of UV radiation-induced by-products in human cataract lenses support the conclusion that oxidative photodegradation is a significant factor in nuclear cataracts (Berendschot et al., 2002). In conclusion, as the vitreous and lens age, the lens nucleus is exposed to higher oxygen concentration and minimal to no antioxidants. A UV-blocking contact lens or spectacles with side shields will limit lens damage through removal of a radiation source, eliminating a “leg” of the oxidative photodegradation triangle.

The retina is the most metabolically active tissue in the body and hence is particularly susceptible to oxidative damage. This exceptional vulnerability to oxidation is due to four primary factors (Gaillard et al., 2011; Hunter et al., 2012; Margrain et al., 2004): 1. Rods and cones are rich in unsaturated fats like DHA and other long chain PUFAs (LCPUFAs) that are prone to oxidation. 2. Blood flow to the retina is poorly regulated, especially in infancy (Hardy et al., 1994) and late in life when receptors are lost (Groh et al., 1996). This can cause excess oxygen in a system already using relatively

high amounts of oxygen. 3. As noted, a high number of photosensitizing compounds accumulate within the retina over time (like lipofuscin (Margrain et al., 2004)). 4. The retina is often exposed to energetic light.

The retina's antioxidant system operates in a highly integrated manner (Lien and Hammond, 2011; Hammond and Lien, 2013; Edge et al., 2007) to protect both aqueous and lipid-soluble components. Vitamin E (in its natural bioavailable form) is an efficient chain-breaking lipid-soluble antioxidant in membranes and plays an essential role in minimizing the oxidation of LCPUFAs. Monkeys fed vitamin E-deficient diets develop macular degeneration, characterized by extensive disruption of the photoreceptor outer segments, most likely due to lipid peroxidation (Hayes, 1974). L and Z are also lipid-soluble antioxidants that quench the triplet state of photosensitizers as well as singlet oxygen, thus they are chain-breaking antioxidants that retard the peroxidation of membrane lipids (Beatty et al., 1999). These carotenoids can return singlet oxygen to the ground state, while they subsequently return to their ground state via a heat-loss process and are prepared for another round of antioxidant activity (Stahl and Sies, 2002). The major water-soluble antioxidant systems of the retina include cytosolic ascorbic acid and a series of enzymes, with their activities primarily in the cellular cytoplasm and mitochondria. Alpha-tocopherol (one of the more biologically active forms of vitamin E) is recycled by redox coupling with vitamin C at the cytosolic/membrane interface (Chaudiere and Ferrari-Iliou, 1999; Sies and Stahl, 1995). Specific antioxidant enzymes directly inhibit superoxide as well as hydroperoxides and provide protection from the generation of ROS. superoxide dismutase (SOD) metabolizes superoxide, while hydroperoxides are metabolized by GPX and catalase. Trace mineral cofactors for cytosolic SOD are zinc and copper, while selenium is an obligatory cofactor for GPX in the human eye (Beatty et al., 1999). Taken together, the entire orbit has an elegant system of antioxidants aimed at reducing the inevitable consequences of photo-oxidative damage.

7. Conclusions

The effects of accumulated light damage on the skin are obvious and highly variable. This variability is observed even for individuals who live close together. The aggregated effects of light and oxygen on ocular structures is even more significant (e.g., damage to nerve structures like the retina is irreversible and untreatable), but cannot be seen, and is equally variable. For the eye and skin, a large proportion of the difference across individuals with similar exposure can be attributed to two major factors: antioxidant intake and the use of filters that screen out energetic UV radiation (ca. 280–400 nm) and visible short-wave light (ca. 400–500 nm), such as hats, sunglasses, sunscreen, or contact lenses. The modern Westernized diet seems particularly deficient in antioxidants that reduce actinic damage. For example, the average intake of lutein and zeaxanthin is about 0.4–1.8 mg/day in Americans (Johnson et al., 2010). The recommended diet, rich in fruits and vegetables, however, would easily provide 20–30 mg/day (Sommerburg et al., 1998). The use of filters to reduce actinic damage is equally variable.

Proteins and lipids are ubiquitous in human cells. Screening of the solar radiation spectrum up to 320 nm ensures minimum oxidative photodegradation of proteins that make up more than 90% of the lens and the majority of the cornea. Screening of radiation from 320 nm to 400 nm reduces oxidative photodegradation in lipids that make up more than 50% of the retina. The majority of the literature supports partial screening of visible light to 500 nm in order to minimize actinic light damage to the retina while maintaining the necessary luminosity for vision. UV-filtering contact lenses might be a particularly good option in that they, unlike most spectacle lenses, filter light from all angles (both above and to the side). Protection from oxidative photodegradation also likely changes with age. Each stage of life represents a different set of vulnerabilities that should be considered. For example, newborns have both low antioxidant protection and exceptionally clear lenses. Children and adults may suffer greater exposure due to more time spent participating in outdoor activities. The elderly may have higher levels of endogenous photosensitizers and reduced ability to metabolize dietary antioxidants.

Unlike many health issues, the approach to reducing oxidative photodegradation is clear and can yield immediate benefit: minimize exposure to actinic light, improve dietary intake of antioxidants (e.g., Lutein and Zeaxanthin), and wear sunglasses and contact lenses that employ maximum protection from UVA and UVB solar radiation.

References

Ablonczy, Z., Higbee, D., Anderson, D.M., Dahrouj, M., Grey, A.C., Gutierrez, D., Crouch, R.K., 2013. Lack of correlation between the spatial distribution of A2E and lipofuscin fluorescence in the human retinal pigment epithelium. Investig. Ophthalmol. Vis. Sci. 54 (8), 5535–5542.

Ablonczy, Z., Smith, N., Anderson, D.M., Grey, A.C., Spraggins, J., Koutalos, Y., Crouch, R.K., 2014. The utilization of fluorescence to identify the components of lipofuscin by imaging mass spectrometry. Proteomics 14 (7–8), 936–944.

Acar, N., Berdeaux, O., Gregoire, S., Cabaret, S., Martine, L., Gain, P., Thuret, G., Creuzot-Garcher, C.P., Bron, A.M., Bretillon, L., 2012. Lipid composition of the human eye: are red blood cells a good mirror of retinal and optic nerve fatty acids? PLoS One 7, e35102.

Algvere, P.V., Marshall, J., Seregard, S., 2006. Age-related maculopathy and the impact of blue light hazard. Acta Ophthalmol. Scand. 84, 4–15.

Anderson, R.E., Rapp, L.M., Wiegand, R.D., 1984. Lipid peroxidation and retinal degeneration. Curr. Eye Res. 3, 223–227.

Andley, U.P., 2009. Effects of α-crystallin on lens cell function and cataract pathology. Curr. Mol. Med. 9 (7), 887–892.

Andley, U.P., Malone, J.P., Townsend, R.R., 2011. Inhibition of lens photodamage by UV-absorbing contact lenses. Investig. Ophthalmol. Vis. Sci. 52 (11), 8330–8341.

Andley, U.P., Malone, J.P., Townsend, R.R., 2014. In vivo substrates of the lens molecular chaperones αA-crystallin and αB-crystallin. PloS One 9 (4), e95507.

Anstey, A., Taylor, D., Chalmers, I., Ansari, E., 1999. Ultraviolet radiation-blocking characteristics of contact lenses: relevance to eye protection for psoralen-sensitised patients. Photodermatol. Photoimmunol. Photomed. 15, 193–197.

Bachem, A., 1956. Ophthalmic action spectra. Am. J. Ophthalmol. 41, 969–975.

Balasubramanian, D., 2000. Ultraviolet radiation and cataract. J. Ocul. Pharmacol. Ther. 16 (3), 285–297.

Barker, F.M., Snodderly, D.M., Johnson, E.J., Schalch, W., Koepcke, W., Gerss, J., Neuringer, M., 2011. Nutritional manipulation of primate retinas, V: effects of lutein, zeaxanthin, and n-3 fatty acids on retinal sensitivity to blue-light-induced damage. Investig. Ophthalmol. Vis. Sci. 52, 3934–3942.

Beatty, S., Boulton, M., Henson, D., Koh, H.H., Murray, I.J., 1999. Macular pigment and age related macular degeneration. Br. J. Ophthalmol. 83, 867–877.

Beebe, D.C., Holekamp, N.M., Siegfried, C., Shui, Y.B., 2011. Vitreoretinal influences on lens function and cataract. Philos. Trans. R. Soc. Lond B Biol. Sci. 366, 1293–1300.

Berendschot, T.T., Broekmans, W.M., Klopping-Ketelaars, I.A., Kardinaal, A.F., Van, P.G., Van, N.D., 2002. Lens aging in relation to nutritional determinants and possible risk factors for age-related cataract. Arch. Ophthalmol. 120, 1732–1737.

Bo, H., Yuesi, W., Guangren, L., 2010. Properties of ultraviolet radiation and the relationship between ultraviolet radiation and aerosol optical depth in China. Atmos. Res. 98, 297–308.

Boettner, E.A., Wolter, J.R., 1962. Transmission of the ocular media. Investig. Ophthalmol. Vis. Sci. 1, 776–783.

Bone, R.A., Landrum, J.T., Hime, G.W., Cains, A., Zamor, J., 1993. Stereochemistry of the human macular carotenoids. Investig. Ophthalmol. Vis. Sci. 34, 2033–2040.

Bone, R.A., Landrum, J.T., Tarsis, S.L., 1985. Preliminary identification of the human macular pigment. Vis. Res. 25, 1531–1535.

Bron, A.J., Vrensen, G.F., Koretz, J., Maraini, G., Harding, J.J., 2000. The ageing lens. Ophthalmologica 214, 86–104.

Carnevale, A., Faez, J., Forteza, J., Valeonti, T., 2012. Do Brands and Prices of Sunglasses Ensure Adequate UV-radiation Protection? (Doctoral dissertation). Available at: http://rudar.ruc.dk:8080/handle/1800/7407 (accessed 24.01.13.).

Carson, D., Margrain, T.H., Patel, A., 2008. New approach to evaluate retinal protection by intraocular lenses against age-related lipofuscin accumulation–mediated retinal phototoxicity. J. Cataract Refract. Surg. 34 (10), 1785–1792.

Chandler, H., 2011. Ultraviolet absorption by contact lenses and the significance on the ocular anterior segment. Eye Contact Lens 37, 259–266.

Chandler, H.L., Reuter, K.S., Sinnott, L.T., Nichols, J.J., 2010. Prevention of UV-induced damage to the anterior segment using class I UV-absorbing hydrogel contact lenses. Investig. Ophthalmol. Vis. Sci. 51, 172–178.
Chao, S.C., Hu, D.N., Yang, P.Y., Lin, C.Y., Nien, C.W., Yang, S.F., Roberts, J.E., 2013. Ultraviolet-A irradiation upregulated urokinase-type plasminogen activator in pterygium fibroblasts through ERK and JNK pathways. Investig. Ophthalmol. Vis. Sci. 54 (2), 999–1007.
Chaudiere, J., Ferrari-Iliou, R., 1999. Intracellular antioxidants: from chemical to biochemical mechanisms. Food Chem. Toxicol. 37, 949–962.
Cherry, J.D., Liu, B., Frost, J.L., Lemere, C.A., Williams, J.P., Olschowka, J.A., O'Banion, M.K., 2012. Galactic cosmic radiation leads to cognitive impairment and increased aβ plaque accumulation in a mouse model of Alzheimer's disease. PloS one 7 (12), e53275.
Coroneo, M., 2011. Ultraviolet radiation and the anterior eye. Eye Contact Lens 37 (4), 214–224.
Cullen, A.P., 2002. Photokeratitis and other phototoxic effects on the cornea and conjunctiva. Int. J. Toxicol. 21, 455–464.
Dahm, R., van, M.J., Quinlan, R.A., Prescott, A.R., Vrensen, G.F., 2011. Homeostasis in the vertebrate lens: mechanisms of solute exchange. Philos. Trans. R. Soc. Lond B Biol. Sci. 366, 1265–1277.
Davies, M.J., Truscott, R.J., 2001. Photo-oxidation of proteins and its role in cataractogenesis. J. Photochem. Photobiol. B 63, 114–125.
Dillon, J., Atherton, S.J., 1990. Time resolved spectroscopic studies on the intact human lens. Photochem. Photobiol. 51 (4), 465–468.
Dillon, J., Zheng, L., Merriam, J.C., Gaillard, E.R., 2004. Transmission of light to the aging human retina: possible implications for age related macular degeneration. Exp. Eye Res. 79, 753–759.
Edge, R., El-Agamey, A., Land, E.J., Navaratnam, S., George Truscott, T., 2007. Studies of carotenoid one-electron reduction radicals. Arch. Biochem. Biophys. 458 (2), 104–110.
Ernest, P.H., 2004. Light-transmission-spectrum comparison of foldable intraocular lenses. J. Cataract Refract. Surg. 30, 1755–1758.
Estey, T., Piatigorsky, J., Lassen, N., Vasiliou, V., 2007. ALDH3A1: a corneal crystallin with diverse functions. Exp. Eye Res. 84, 3–12.
Fecondo, J.V., Augusteyn, R.C., 1983. Superoxide dismutase, catalase and glutathione peroxidase in the human cataractous lens. Exp. Eye Res. 36, 15–23.
Fisher, R.F., Pettet, B.E., 1973. Presbyopia and the water content of the human crystalline lens. J. Physiol. 234, 443–447.
Gaillard, E.R., Merriam, J., Zheng, L., Dillon, J., 2011. Transmission of light to the young primate retina: possible implications for the formation of lipofuscin. Photochem. Photobiol. 87, 18–21.
Gao, J., Sun, X., Moore, L.C., White, T.W., Brink, P.R., Mathias, R.T., 2011. Lens intracellular hydrostatic pressure is generated by the circulation of sodium and modulated by gap junction coupling. J. Gen. Physiol. 137 (6), 507–520.
Glickman, R.D., 2011. Ultraviolet phototoxicity to the retina. Eye Contact Lens 37, 196–205.
Groh, M.J., Michelson, G., Langhans, M.J., Harazny, J., 1996. Influence of age on retinal and optic nerve head blood circulation. Ophthalmology 103 (3), 529–534.
Hammond Jr., B.R., Wooten, B.R., Snodderly, D.M., 1997. Individual variations in the spatial profile of human macular pigment. J. Opt. Soc. Am. A Opt. Image Sci. Vis. 14, 1187–1196.
Hammond Jr., B.R., Wooten, B.R., Snodderly, D.M., 1998. Preservation of visual sensitivity of older subjects: association with macular pigment density. Investig. Ophthalmol. Vis. Sci. 39, 397–406.
Hammond, B.R., Lien, E., 2013. Dietary prevention and treatment of ocular disease. Duane's Atlas Ophthalmol. 34 (3), 1–25.
Hardy, P., Abran, D., Li, D.Y., Fernandez, H., Varma, D.R., Chemtob, S., 1994. Free radicals in retinal and choroidal blood flow autoregulation in the piglet: interaction with prostaglandins. Investig. Ophthalmol. Vis. Sci. 35 (2), 580–591.
Hayes, K.C., 1974. Retinal degeneration in monkeys induced by deficiencies of vitamin E or A. Investig. Ophthalmol. 13, 499–510.
Held, P., 2003. Quantitation of Peptides and Amino Acids with a Synergy™HT Using UV Fluorescence. BioTek Application Note.
Henderson, B.A., Grimes, K.J., 2010. Blue-blocking IOLs: a complete review of the literature. Surv. Ophthalmol. 55, 284–289.
Hunter, J.J., Morgan, J.I., Merigan, W.H., Sliney, D.H., Sparrow, J.R., Williams, D.R., 2012. The susceptibility of the retina to photochemical damage from visible light. Prog. Retin. Eye Res. 31, 18–42.
Ibrahim, O.M., Kojima, T., Wakamatsu, T.H., Dogru, M., Matsumoto, Y., Ogawa, Y., Ogawa, J., Negishi, K., Shimazaki, J., Sakamoto, Y., Sasaki, H., Tsubota, K., 2012. Corneal and retinal effects of ultraviolet-B exposure in a soft contact lens mouse model. Investig. Ophthalmol. Vis. Sci. 53, 2403–2413.
Johnson, E.J., Maras, J.E., Rasmussen, H.M., Tucker, K.L., 2010. Intake of lutein and zeaxanthin differ with age, sex, and ethnicity. J. Am. Diet. Assoc. 110 (9), 1357–1362.
Karppi, J., Laukkanen, J.A., Kurl, S., 2012. Plasma lutein and zeaxanthin and the risk of age-related nuclear cataract among the elderly Finnish population. Br. J. Nutr. 108, 148–154.
Kelen, T., 1983. Polymer Degradation. Van Nostrand Reinhold Co.
Khan, A., Wilson, T., 1995. Reactive oxygen species as cellular messengers. Chem. Biol. 2 (7), 437–445.
Klein, R., Chou, C.F., Klein, B.E., Zhang, X., Meuer, S.M., Saaddine, J.B., 2011. Prevalence of age-related macular degeneration in the US population. Arch. Ophthalmol. 129, 75–80.
Kohnen, T., 2009. How far we have come: from Ridley's first intraocular lens to modern IOL technology. J. Cataract Refract. Surg. 35, 2039.
Kremers, J.J.M., Van Norren, D., 1988. Two classes of photochemical damage of the retina. Lasers Light Ophthalmol. 2 (1), 41–52.
Lampi, K.J., Wilmarth, P.A., Murray, M.R., David, L.L., 2014. Lens β-crystallins: the role of deamidation and related modifications in aging and cataract. Prog. Biophys. Mol. Biol. 115 (1), 21–31.
Lien, E.L., Hammond, B.R., 2011. Nutritional influences on visual development and function. Prog. Retin. Eye Res. 30, 188–203.
Lin, K.K., Lin, Y.C., Lee, J.S., Chao, A.N., Chen, H.S.L., 2002. Spectral transmission characteristics of spectacles, contact lenses, and intraocular lenses. Ann. Ophthalmol. 34, 206–215.
Lira, M., Dos Santos Castanheira, E.M., Santos, L., Azeredo, J., Yebra-Pimentel, E., Real Oliveira, M.E., 2009. Changes in UV-visible transmittance of silicone-hydrogel contact lenses induced by wear. Optom. Vis. Sci. 86, 332–339.
Loan, F.A., Winslow, F.H., 1979. Reactions of macromolecules. In: Bovey, F.A., Winslow, F.H. (Eds.), Macromolecules-an Introduction to Polymer Science. Academic Press, New York, NY.
Lucas, R.M., 2011. An epidemiological perspective of ultraviolet exposure–public health concerns. Eye Contact Lens 37, 168–175.
Mainster, M.A., Turner, P.L., 2011. Blue-blocking IOLs vs. short-wavelength visible light: hypothesis-based vs. evidence-based medical practice. Ophthalmology 118, 1–2.
Margrain, T.H., Boulton, M., Marshall, J., Sliney, D.H., 2004. Do blue light filters confer protection against age-related macular degeneration? Prog. Retin. Eye Res. 23, 523–531.
Mathias, R.T., White, T.W., Gong, X., 2010. Lens gap junctions in growth, differentiation, and homeostasis. Physiol. Rev. 90, 179–206.
McKinlay, A.F., Diffey, B.L., 1987. Human Exposure to Ultraviolet Radiation: Risks and Regulations. Excerpta Medica, Amsterdam, Netherlands.
McLaren, J.W., Dinslage, S., Dillon, J.P., Roberts, J.E., Brubaker, R.F., 1998. Measuring oxygen tension in the anterior chamber of rabbits. Investig. Ophthalmol. Vis. Sci. 39 (10), 1899–1909.
Mecherikunnel, A.T., Richmond, J., 1980. Spectral distribution of solar radiation. NASA STI/Recon Technical Report N 81, 25028.
Merriam, J.C., 1996. The concentration of light in the human lens. Trans. Am. Ophthalmol. Soc. 94, 803–918.
Michael, R., Bron, A.J., 2011. The ageing lens and cataract: a model of normal and pathological ageing. Philos. Trans. R. Soc. Lond B Biol. Sci. 366, 1278–1292.
Miquel, J., Ramirez-Bosca, A., Soler, A., Diez, A., Carrion-Gutierrez, M.A., az-Alperi, J., Quintanilla-Ripoll, E., Bernd, A., Quintanilla-Almagro, E., 1998. Increase with age of serum lipid peroxides: implications for the prevention of atherosclerosis. Mech. Ageing Dev. 100, 17–24.
Norren, D.V., Vos, J.J., 1974. Spectral transmission of the human ocular media. Vis. Res. 14, 1237–1244.
Norval, M., Cullen, A.P., De Gruijl, F.R., Longstreth, J., Takizawa, Y., Lucas, R.M., Van der Leun, J.C., 2007. The effects on human health from stratospheric ozone depletion and its interactions with climate change. Photochem. Photobiol. Sci. 6 (3), 232–251.
Norval, M., 2011. The mechanisms and consequences of ultraviolet-induced immunosuppression in the skin and eye. Eye Contact Lens 37, 176–184.
Parker, N.R., Jamie, J.F., Davies, M.J., Truscott, R.J., 2004. Protein-bound kynurenine is a photosensitizer of oxidative damage. Free Radic. Biol. Med. 37, 1479–1489.
Pattison, D.I., Rahmanto, A.S., Davies, M.J., 2012. Photo-oxidation of proteins. Photochem. Photobiol. Sci. 11, 38–53.
Perrone, S., Longini, M., Marzocchi, B., Picardi, A., Bellieni, C.V., Proietti, F., Rodriguez, A., Turrisi, G., Buonocore, G., 2010. Effects of lutein on oxidative stress in the term newborn: a pilot study. Neonatology 97, 36–40.
Pitts, D.G., Tredici, T.J., 1971. The effects of ultraviolet on the eye. Am. Ind. Hyg. Assoc. J. 32, 235–246.
Pitts, D.G., Cullen, A.P., 1981. Determination of infrared radiation levels for acute ocular cataractogenesis. Albr. Graefes Arch. klin. exp. Ophthalmol. 217, 285–297.
Pokorny, J., Smith, V.C., Lutze, M., 1987. Aging of the human lens. Appl. Opt. 26, 1437–1440.
Porter, N.A., 1986. Mechanisms for the autoxidation of polyunsaturated lipids. Acc. Chem. Res. 19, 262–268.
Porter, N.A., Caldwell, S.E., Mills, K.A., 1995. Mechanisms of free radical oxidation of unsaturated lipids. Lipids 30, 277–290.
Pratt, D.A., Tallman, K.A., Porter, N.A., 2011. Free radical oxidation of polyunsaturated lipids: new mechanistic insights and the development of peroxyl radical clocks. Acc. Chem. Res. 44, 458–467.
Rezai, K.A., Gasyna, E., Seagle, B.L., Norris Jr., J.R., Rezaei, K.A., 2008. AcrySof Natural filter decreases blue light-induced apoptosis in human retinal pigment epithelium. Graefe's Arch. Clin. Exp. Ophthalmol. 246, 671–676.
Roberts, J.E., Wishart, J.F., Martinez, L., Chignell, C.F., 2000. Photochemical studies on xanthurenic acid. Photochem. Photobiol. 72 (4), 467–471.
Roberts, J.E., Finley, E.L., Patat, S.A., Schey, K.L., 2001. Photooxidation of lens proteins with xanthurenic acid: a putative chromophore for cataractogenesis. Photochem. Photobiol. 74 (5), 740–744.
Roberts, J.E., 2001. Ocular phototoxicity. J. Photochem. Photobiol. B Biol. 64 (2), 136–143.
Roberts, J.E., Kukielczak, B.M., Hu, D.N., Miller, D.S., Bilski, P., Sik, R.H., Chignell, C.F., 2002. The role of A2E in prevention or Enhancement of light damage in human retinal pigment epithelial cells. Photochem. Photobiol. 75 (2), 184–190.

Roberts, J.E., 2011. Ultraviolet radiation as a risk factor for cataract and macular degeneration. Eye Contact Lens 37 (4), 246–249.
Rosenthal, et al., 1988. The ocular dose of UVR to outdoor workers. Investig. Ophthalmol. Vis. Sci. 29 (4), 649.
Różanowska, M., Wessels, J., Boulton, M., Burke, J.M., Rodgers, M.A., Truscott, T.G., Sarna, T., 1998. Blue light-induced singlet oxygen generation by retinal lipofuscin in non-polar media. Free Radic. Biol. Med. 24 (7), 1107–1112.
Sample, P.A., Esterson, F.D., Weinreb, R.N., 1989. A practical method for obtaining an index of lens density with an automated perimeter. Investig. Ophthalmol. Vis. Sci. 30, 786–787.
Sasaki, H., Sakamoto, Y., Schnider, C., Fujita, N., Hatsusaka, N., Sliney, D.H., Sasaki, K., 2011. UV-B exposure to the eye depending on solar altitude. Eye Contact Lens 37, 191–195.
Savage, G.L., Johnson, C.A., Howard, D.L., 2001. A comparison of noninvasive objective and subjective measurements of the optical density of human ocular media. Optom. Vis. Sci. 78, 386–395.
Schmidt, R.E., Zuclich, J.A., 1980. Retinal lesions due to ultraviolet laser exposure. Investig. Ophthalmol. Vis. Sci. 19 (10), 1166–1175.
Shao, W., Zhang, S.Z., Tang, M., Zhang, X.H., Zhou, Z., Yin, Y.Q., Zhou, Q.B., Huang, Y.Y., Liu, Y.J., Wawrousek, E., Chen, T., Li, S.B., Xu, M., Zhou, J.N., Hu, G., Zhou, J.W., 2013. Suppression of neuroinflammation by astrocytic dopamine D2 receptors via alphaB-crystallin. Nature 494, 90–94.
Sherwin, J.C., Reacher, M.H., Keogh, R.H., Khawaja, A.P., Mackey, D.A., Foster, P.J., 2012. The association between time spent outdoors and myopia in children and adolescents: a systematic review and meta-analysis. Ophthalmology 119 (10), 2141–2151.
Sies, H., Stahl, W., 1995. Vitamins E and C, beta-carotene, and other carotenoids as antioxidants. Am. J. Clin. Nutr. 62, 1315S–1321S.
Sliney, D.H., 2011. Intraocular and crystalline lens protection from ultraviolet damage. Eye Contact Lens 37, 250–258.
Sommerburg, O., Keunen, J.E., Bird, A.C., van Kuijk, F.J., 1998. Fruits and vegetables that are sources for lutein and zeaxanthin: the macular pigment in human eyes. Br. J. Ophthalmol. 82 (8), 907–910.
Sparrow, J.R., Miller, A.S., Zhou, J., 2004. Blue light-absorbing intraocular lens and retinal pigment epithelium protection in vitro. J. Cataract Refract. Surg. 30, 873–878.
Spikes, J.D., MacKnight, M.L., 2006. Dye-sensitized photoxidation of proteins*. Ann. N. Y. Acad. Sci. 171, 149–162.
Stahl, W., Sies, H., 2002. Carotenoids and protection against solar UV radiation. Skin Pharmacol. Appl. Skin. Physiol. 15, 291–296.
Stone, E.M., 2007. Macular degeneration. Annu. Rev. Med. 58, 477–490.
Sui, G.Y., Liu, G.C., Liu, G.Y., Gao, Y.Y., Deng, Y., Wang, W.Y., Tong, S.H., Wang, L., 2013. Is sunlight exposure a risk factor f or age-related macular degeneration? A systematic review and meta-analysis. Br. J. Ophthalmol. 97, 389–394.
Sujak, A., Okulski, W., Gruszecki, W.I., 2000. Organisation of xanthophyll pigments lutein and zeaxanthin in lipid membranes formed with dipalmitoylphosphatidylcholine. Biochim. Biophys. Acta 1509, 255–263.
Sweeney, M.H., Truscott, R.J., 1998. An impediment to glutathione diffusion in older normal human lenses: a possible precondition for nuclear cataract. Exp. Eye Res. 67, 587–595.
Sydenham, M.M., Collins, M.J., Hirst, L.W., 1997. Measurement of ultraviolet radiation at the surface of the eye. Investig. Ophthalmol. Vis. Sci. 38 (8), 1485–1492.
Tang, P.H., Kono, M., Koutalos, Y., Ablonczy, Z., Crouch, R.K., 2013. New insights into retinoid metabolism and cycling within the retina. Prog. Retin. Eye Res. 32, 48–63.
Trozzolo, A.M., 1972. Stabilization against oxidative photodegradation. In: Hawkins, W.L. (Ed.), Polymer Stabilization. Wiley-Interscience, New York, NY.
Truscott, R.J., 2000. Age-related nuclear cataract: a lens transport problem. Ophthalmic research 32 (5), 185–194.
Truscott, R.J., 2009. Presbyopia. Emerging from a blur towards an understanding of the molecular basis for this most common eye condition. Exp. Eye Res. 88, 241–247.
Truscott, R.J., Mizdrak, J., Friedrich, M.G., Hooi, M.Y., Lyons, B., Jamie, J.F., Davies, M.J., Wilmarth, P.A., David, L.L., 2012. Is protein methylation in the human lens a result of non-enzymatic methylation by S-adenosylmethionine? Exp. Eye Res. 99, 48–54.
van de Kraats, J., van Norren, D., 2007a. Optical density of the aging human ocular media in the visible and the UV. J. Opt. Soc. Am. A Opt. Image. Sci. Vis. 24, 1842–1857.
van de Kraats, J., van Norren, D., 2007b. Sharp cutoff filters in intraocular lenses optimize the balance between light reception and light protection. J. Cataract Refract. Surg. 33 (5), 879–887.
van Norren, D., Gorgels, T.G., 2011. The action spectrum of photochemical damage to the retina: a review of monochromatic threshold data. Photochem. Photobiol. 87 (4), 747–753.
Velpandian, T., Ravi, A.K., Kumari, S.S., Biswas, N.R., Tewari, H.K., Ghose, S., 2005. Protection from ultraviolet radiation by spectacle lenses available in India: a comparative study. Natl. Med. J. India 18, 242–244.
Vishwanathan, R., Chung, M., Johnson, E.J., 2013. A systematic review on zinc for the prevention and treatment of age-related macular degeneration. Investig. Ophthalmol. Vis. Sci. 54, 3985–3998.
Voke, J., 1999. Radiation effects on the eye, part 1: infrared radiation effects on ocular tissue. Optom. Today 5, 22–28.
Waiblinger, F., Keck, J., Fluegge, A.P., Kramer, H.E., Leppard, D., Rytz, G., 1999. Ultraviolet absorbers and singlet oxygen. J Photochem. Photobiol. A Chem. 126, 43–49.
Wald, G., 1945. Human vision and the spectrum. Science 101, 653–658.
Walsh, J.E., Bergmanson, J.P., 2011. Does the eye benefit from wearing ultraviolet-blocking contact lenses? Eye Contact Lens 37, 267–272.
Weale, R.A., 1988. Age and the transmittance of the human crystalline lens. J. Physiol. 395 (1), 577–587.
Werner, J.S., 1982. Development of scotopic sensitivity and the absorption spectrum of the human ocular media. J. Opt. Soc. Am. 72, 247–258.
Werner, J.S., Spillmann, L., 1989. UV-absorbing intraocular lenses: safety, efficacy, and consequences for the cataract patient. Graefe's Arch. Clin. Exp. Ophthalmol. 227, 248–256.
Wielgus, A.R., Roberts, J.E., 2012. Retinal photodamage by endogenous and xenobiotic agents†. Photochem. Photobiol. 88 (6), 1320–1345.
Winslow, F.H., 1977. Photooxidation of high polymers. Pure Appl. Chem. 49, 495–502.
Wyszecki, G., Stiles, W.S., 1982. Color Science. Wiley, New York, NY, pp. 102–103.
Yang, H., Afshari, N.A., 2014. The yellow intraocular lens and the natural ageing lens. Curr. Opin. Ophthalmol. 25 (1), 40–43.
Yeum, K.J., Taylor, A., Tang, G., Russell, R.M., 1995. Measurement of carotenoids, retinoids, and tocopherols in human lenses. Investig. Ophthalmol. Vis. Sci. 36, 2756–2761.
Young, R.W., 1992. Sunlight and age-related eye disease. J. Natl. Med. Assoc. 84, 353–358.
Zuclich, J.A., 1989. Ultraviolet-induced photochemical damage in ocular tissues. Health Phys. 56, 671–682.